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PRIMARY MALIGNANT TUMORS OF THE OVARY

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THIS paper is an attempt to clarify the relationship between the clinicopathological picture of primary malignant neoplasms of the ovary and the therapeutic end-results. It is based on a study of 92 patients who have been admitted to this Institute for diagnosis and treatment. Only those cases in which pathological material is now available for review have been selected.

The ovary, being an organ of both extrinsic and intrinsic function, plays an important rôle in the vital metabolism of the body. Its origin, development, and subsequent gross and histological transformations present a complex background in the interpretation of the various malignant growths which affect it. The divergent theories of origin and development of these neoplasms find their champions with proof of both plausible and fantastic accuracy.

Some observers believe that normal somatic cells may change gradually through a benign neoplasm into a malignant growth. Stevens denies this possibility of the supervention of cancer in an innocent neoplasm. Sampson has suggested that endometrial cysts may be precancerous lesions and presented evidence in 7 of 16 ovarian cancers examined. He described endometrium-like tissue in the site of the malignancy. Taylor could not find even the smallest indication of a practical or theoretical structural ground for a separation of an "endometrial carcinoma" from the germinal epithelium carcinoma of the ovary. This germinal epithelium, which Maximow derives from mesothelium and Fischel claims arises from mesenchyme, gives rise to structures which may be both intra-ovarian and extra-ovarian. Certain of the structures remain after birth either in a functional capacity or as atrophied remnants in the ovary itself, the mesovarian, or in the broad ligament.

It does seem reasonable that cells or groups of cells normally found in the ovary may undergo malignant changes with all the possibilities of structural and morphological transformations seen in tumors of much simpler origin. The rare occurrence of extra-ovarian tissues in the ovary and the bizarre cellular growths resulting from embryonal rests and ovulogenic tumors is admitted. But these are the exceptions and not the rule in the origin of most ovarian neoplasms.

The tumors of this series are divided into three main groups, namely: (1) adenocarcinoma, (2) carcinoma, and (3) embryoma.

The question of a tumor being cystic or solid has had no real bearing on this classification. As Taylor has pointed out, "true solid tumors are extremely rare and seem as a rule to be of teratomatous or sarcomatous nature."

The structure of the neoplasm and the morphology of stroma and epithelium have been the deciding factors. Suffice it to say that not all sections of the same growth are identical. One may see a change from cystic papillary

structure to almost diffuse epithelial tumefaction. Metaplasia of cells increases the difficulty of accurate identification. But the predominant and most constant cellular characteristics have determined our final decision.

The division into three main groups not only simplifies a most complex problem, but also provides a working basis in the interpretation of the therapeutic end-results.

PATHOLOGY

1. Under *adenocarcinoma* are grouped those tumors showing true gland-like formations, with or without papillary structures. Microscopically they exhibited both semimalignant and complete malignant characteristics. In a few the proliferation of epithelial cells was scant but sufficiently irregular and hyperchromatic to justify their classification under malignancy (Fig. 1). Many presented a dense stroma with invasion by surface cells (Fig. 2). Numerous mitoses, round cell infiltration, hyperchromaticism, obliteration of cystic cavities by diffuse sheaths of cells (Fig. 3), together with pseudo-alveolar spaces formed by liquefaction necrosis (Fig. 4), furnished a variety of histological pictures. Bell concludes an accurate description of the malignant papillary neoplasms by saying "often the stroma is clear and the epithelium pleomorphic." Cystic cavities may contain either mucoid (Fig. 5) or serous secretions. This mucoid type of cell does not necessarily indicate a muellerian duct rest or an entodermal component of an embryoma. Germinal epithelium may be responsible.

2. Since hardly two *carcinoma* cases resembled one another, a subdivision into four types seems necessary.

a. Under the *medullary* type are grouped those cases presenting anastomosing columns of epithelial cells which may vary as to size, shape, and staining characteristics. The stroma may be dense and cellular or loose with mucoid degeneration (Fig. 6). One may see cells like ova, which Ewing attributes to mucoid degeneration, and sheaths of squamous cells produced by metaplasia. Cystic areas when found are due usually to liquefaction and necrosis. The presence of goblet cells in the ovary does not necessarily indicate a metastatic tumor or fetal muellerian-duct rests. Walthard has demonstrated their presence in small islands in many otherwise normal ovaries and attributes them to metaplasia of germinal epithelium.

b. *Alveolar* formation of cells varies in all histological aspects from small round cells with deeply staining granular protoplasm arranged about an indefinite lumen (Fig. 7) and resembling lymphosarcoma, to larger, clearer and more irregular cells arranged about a more definite lumen. The stroma is as variable as in the medullary type and may closely resemble a mesoblastic tumor of almost any variety.

c. *Granulosa cell* carcinomas are not common and are relatively benign because they are very often permanently cured by removal (Taussig). They consist of cells closely related to the granulosa cells and are classified by Carl Sternberg as epithelial tumors. Their origin from embryonic rests of ovarian parenchyma in the medulla of the ovary has been voiced by TeLinde. King has stated: "they possibly arise from cells in the ovary which are the progenitors of these follicular cells." According to Fischel both the granulosa and the stroma are formed by the ovarian mesenchyme. Novak states: "in either event the kinship of the two tissues is so close that tumors arising in the early stages of differentiation may assume the type of either carcinoma or sarcoma." Histologically they usually present a very constant picture. Masses of regular clear cells which resemble the granulosa cells of the graafian follicle, are arranged in a fairly loose formation about spaces which are often filled with bloody material (Fig. 8). A typical cylindrical formation of these cells is often present (cylindroid epithelioma, Fig. 9). A very unripe type of cellular formation may be present, which may closely resemble a sarcoma (Fig. 10). Careful examination, however, will reveal the epithelial character and attempt at typical grouping on the part of the malignant cells. Also scattered throughout the tumor may be seen spaces resembling the Call and Exner bodies and theca folliculi. Novak described cells resembling secretory cells and decidua in two granulosa cell tumors, one reported by Arnold et al. and the other by Dworzak.

Fig. 1. Papillary cystadenocarcinoma showing early malignant changes. Case 9095; age, 27 years; married; primipara; alive and well 8½ years after bilateral ovariectomy and irradiation.

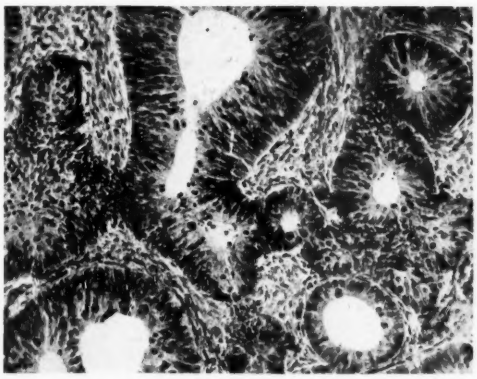

Fig. 2. Adenocarcinoma. Case 15588; age, 30 years; single; nullipara; died 10 months after bilateral cystic ovarian tumors were removed and irradiation therapy begun.

d. The *embryonal cell carcinoma* (seminoma ovarii) resembles in many ways the related type found in the testis. In some respects it may be hard to differentiate histologically from the diffuse unripe granulosa cell carcinoma. Two of our 3 cases were of this sort. Careful examination, however, failed to reveal the grouping of cells in the fashion which is so diagnostic of the granulosa cell carcinoma. Diffuse masses of epithelial cells of a definite embryonal character with little or no stroma and obliteration of ovarian structure predominated the picture (Fig. 11).

Clinically this tumor does not induce any changes in the primary or secondary sex characteristics as compared to definite clinical syndromes often associated with granulosa cell carcinoma and arrhenoblastoma.

3. *Embryoma* represents a group of neoplasms composed of heterogeneous tissue elements. Shattock stated that an embryoma may be due to the fertilization of one of the primordial ova in the ovary of the developing embryo, the result being that the embryo gives rise to a second imperfect individual whose origin is not synchronous with itself but is of a later date.

Marchand theorized the possibility of the fertilization and development of polar bodies although there is practically no evidence in its favor, and MacCallum states that there may be multiple teratomatous tumors which could not be explained on this basis, since at most there are two polar bodies. The latter author believes that the evidence in favor of the isolation of a blastomere as the origin of teratomatous tumors is much stronger than the preceding theories. It is the only type of tumor in which a true mixed carcinoma and sarcoma may exist (Heinrich). They are usually unilateral although 2 of our 7 cases were bilateral when operation was done. This may be due to metastasis of the malignant cells from one ovary to the other. Wilms considered solid embryoma as originally benign, only secondarily showing malignant changes, while Pfannenstiel, Ewing, Boyd considered these tumors malignant from the beginning.

The 7 cases in this series showed histological characteristics of several types. Spindle cell sarcomas (Fig. 12 D), myosarcomas (Fig. 12 A), myxosarcoma (Fig. 13), adenocarcinoma (Fig. 14 A), and medullary carcinomas were found. The possibility of metaplasia was carefully ruled out. Usually one type of cellular structure predominated, but the presence of bizarre combinations and the apparent mixed type of involvement satisfied us as to their ovulogenic origin.

INCIDENCE

An accurate figure cannot be given as to the incidence of primary ovarian malignancies. Reports from the literature are confusing due to the differences in classification, especially

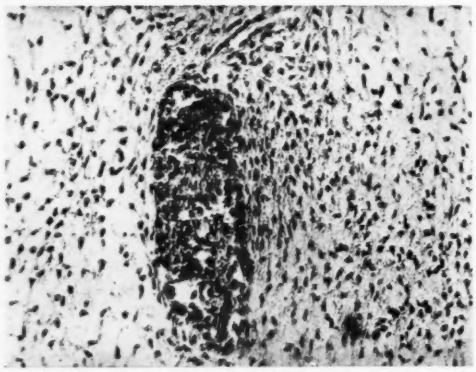

Fig. 3. Adenocarcinoma. Highly malignant cells filling a cystic area in a loose and mucoid-like stroma. Case 1312; age, 42 years; married; multipara 2; died 4 months after palliative operation and 3 months after irradiation therapy was begun.

of the semimalignant or borderline cases. Stout at the Presbyterian Hospital found 5.3 per cent of all female cancer to be ovarian. Norris and Murphy (19) reported that their ovarian neoplasms constituted 7.7 per cent of all gynecological lesions of which 14 per cent were malignant. Percentages of incidence of malignancy in ovarian tumors by five different observers varied from 7.3 to 24.2 (7, 12, 13, 17, 20).

No attempt has been made to determine the incidence in this Institute. Many cases have been admitted and treated which are not here reported because pathological material is not available for study.

AGE

No age is excepted in the development of a malignant neoplasm of the ovary.

Three carcinoma patients less than 20 years of age have been treated at this Institute, the youngest patient being 11 years old. The incidence of ovarian cancer is highest in the fifth and sixth decades of life. Between 40 and 59 years of age our incidence is 55.4 per cent.

Of our cases 39.7 per cent had had a natural menopause when admitted and 9.68 per cent had had a cessation of menses due to operation.

Our cases are grouped as in Table I. It is notable that 88.2 per cent of the adenocarcinoma group occurred after 30 years of age,

TABLE I.—AGE INCIDENCE

Group	10–15	16–20	21–25	26–29	30–39	40–49	50–59	60–
Adenocarcinoma		1	2	5	6	24	18	1
Carcinoma	2	1	2	1	3	7	2	
Embryoma			1	1	4			
Total	2	2	5	7	13	31	20	1
Total per cent	17.3				47.8		34.6	
Group per cent								
Adenocarcinoma	50				68.1		93.7	
Carcinoma	37.5				22.7		6.3	
Embryoma	12.5				9.0			

	Adeno-carci-noma	Carci-noma	Embry-oma	Total
Group 10–29 years, per cent	11.7	33.3	28.5	
Group 30–49 years, per cent	44.1	55.5	66.6	
Group 50–69 years, per cent	44.1	11.1		
Average age—in years	45.8	35	31.6	37.4
Youngest in years	16	11	23	11
Oldest in years	69	53	38	69

that number being equally divided in the 30 to 49 and 50 to 69 age periods. Of the carcinoma group 55.5 per cent occurred in the 30 to 49 year period while 33.3 per cent happened under 30 years. The greatest percentage (66.6) of the embryomas occurred between the ages of 30 and 49. All of the 6 cases were under 39 years.

Age statistics in the carcinoma group are:

Type	Average years	Oldest years	Youngest years
Medullary	36	46	20
Alveolar	41	51	33
Granulosa	33	53	11
Embryonal	31	41	23

Of the total number of cases under 30 years (17.3 per cent) the adenocarcinomas lead with 50.0 per cent. Embryomas make up only 12.5 per cent of this group and carcinomas 37.5 per cent.

The average age of the adenocarcinoma group is 45.8 years. This is 10.8 years higher than a corresponding figure for the carcinoma group and 14.2 years' increase over the embryoma group.

A history of malignancy in the immediate blood relations was present in 7 adenocarcinoma cases (10.2 per cent) and 1 embryoma case (16.6 per cent).

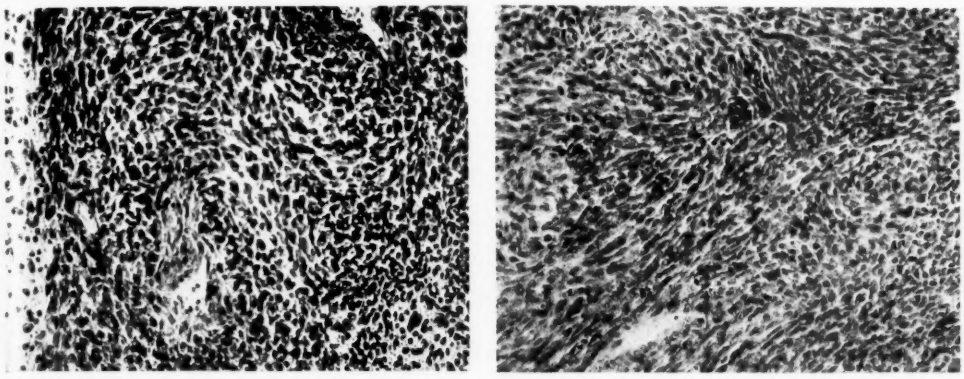

Fig. 4. Both pictures show diffuse mass of round and spindle shaped cells in the wall of tumor and also pseudo-alveolar areas. Other sections showed typical adenocarcinomatous structures. Case 1366; age, 58 years; single; nullipara; died 3 months after palliative operation for bilateral ovarian adenocarcinoma and 3 months after irradiation.

MARRIAGE AND PREGNANCY

Our statistics (Table II) show that of the total number 73.9 per cent are married. The figures for the individual groups vary from 61.1 per cent (carcinoma) to 83.3 per cent (embryoma) with the adenocarcinoma group having a percentage of 76.5.

In 34.7 per cent of our cases patients were never pregnant. In this respect the carcinoma group leads with a percentage of 38.8. Sixteen adenocarcinoma cases (23.5 per cent) and one embryoma case (16.6 per cent) were sterile in marriage. The largest number of pregnancies were:

Group	Greatest number	Average
Adenocarcinoma	5	2
Carcinoma	10	4
Embryoma	6	4

A comparison of the four types of carcinoma follows:

Type	Cases	Single	Married	Nullipara	Primipara	Multipara
Medullary	4	2	2	2	1	1
Alveolar	4	1	3	1	0	3
Granulosa cell	7	4	3	4	0	3
Embryona lcell	3	0	3	0	1	2

Abortions and miscarriages which in the great majority were apparently not induced, occurred in 23.5 per cent of the adenocarcinoma and 16.6 per cent of the embryoma and carcinoma groups. Of the last group (3 cases), 1 occurred in an alveolar type and the other 2 in the granulosa cell type (66.6 per cent of the married cases).

Only two stillbirths were recorded. One was an alveolar carcinoma and the other an embryonal cell type of carcinoma.

These figures testify as to the functional activity of the ovaries both in a normal and abnormal fashion.

SYMPTOMS AND SIGNS

Clinically these tumors presented a marked variety of symptoms and signs. None is in itself absolute for diagnosis. Only pathological study determines definitely their malignant qualities, although at operation one may identify cancer in many cases.

The prediagnostic length of symptoms averages about the same in all groups.

Name	Average months	Longest years	Shortest month
Adenocarcinoma	15	20	1
Carcinoma	11.6	3	1
Embryoma	13.5	2.5	1

Kaplan reported that the average duration of symptoms of ovarian malignancy in his series is 10 months with 1 case of 12 years.

Pain in the abdomen is the most outstanding symptom. Frequently it is hypogastric in type and many times is associated with nausea and emesis. Swelling of the abdomen is quite prevalent as are backaches, bearing-down sensations in pelvis, and frequent and painful micturition. Loss of weight is often

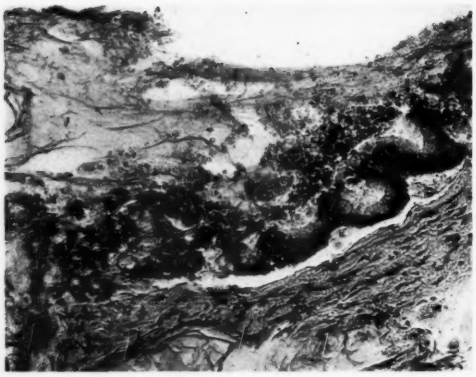

Fig. 5. Adenocarcinoma, mucoid type (radioresistant). Case 11179; age, 43 years; married; multipara 2; died 1 year, 10 months after palliative operation for ovarian tumor mass and commencement of irradiation.

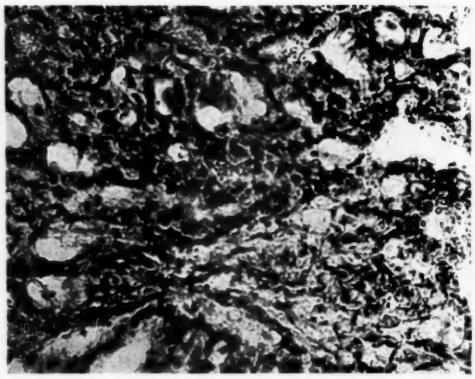

Fig. 6. Medullary carcinoma with mucoid degeneration. Case 16062; age, 20 years; single; nullipara; died 1½ years after right ovarian tumor was removed and 1 year after irradiation was begun.

marked. Menstrual irregularities with increased or decreased flow are not so frequent as a large percentage of patients are past the menopause. In these cases one often sees bloody vaginal discharge. When this postmenopausal bleeding is of the endometrium and more especially if it is periodic in character, granulosa cell tumor of the ovary must be entertained. In this series 30.4 per cent had passed an apparently normal menopause when symptoms began. Mullerheim has reported 2 cases of ovarian cancer in women aged 69 and 72 years who had swelling of both breasts. We have not noticed this in our cases. Precocious puberty with aggravation of secondary sexual characteristics may be seen in granulosa cell carcinoma in young girls. Two of our patients, 11 and 14 years of age, began menstruating when 11 and 12 years old, respectively, with early pubertal characteristics.

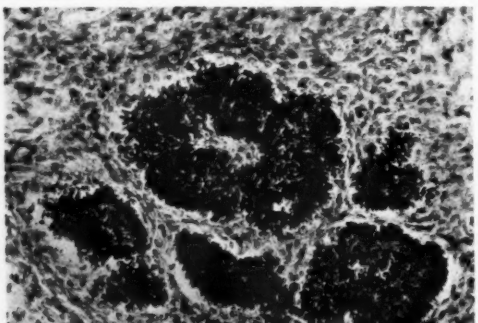

Fig. 7. Alveolar carcinoma. Small round anaplastic epithelial cells resembling in some sections lymphosarcoma. Attempt at an arrangement about an indefinite lumen. Case 15302; age, 33 years; married, multipara 3; died 1 year after irradiation was begun and 1 month after diagnostic operation.

A comparison of clinical data in the three main divisions is interesting (Table III).

Pain in the abdomen was an outstanding complaint in 83.3 per cent of the embryoma cases and 77.7 per cent of the carcinoma cases, while enlargement of the abdomen showed a percentage incidence of 16.6 per cent and 27.7 per cent, respectively. The adenocarcinoma group differed quite markedly in that the percentage of incidence of abdominal pain was 55.8 per cent and of enlargement of the abdomen 44.1 per cent. This latter complaint showed as either a diffuse growth or expansion of the abdomen with fullness, or else as a more unilateral suprapelvic enlargement.

Nausea, emesis, and backache were much more frequent in the carcinoma and embryoma groups. No histories of urinary disturbances were obtained in the embryoma cases but 22.5 per cent of the carcinoma and 14.7 per cent of the adenocarcinoma cases complained of frequent and painful micturition. Whitehouse cites the occurrence of painful as well as frequent urination as a differen-

TABLE II.—MARRIAGE, PREGNANCY, MENOPAUSE

	Adenocarcinoma		Carcinoma		Embryoma		Total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Single	16	23.5	7	38.8	1	16.6	24	26.0
Married	52	76.5	11	61.1	5	83.3	68	73.9
Primipara	12	17.6	2	11.1	1	16.6	15	16.3
Multipara	24	35.2	9	50.0	3	50.0	36	39.1
No pregnancies — single and sterile cases	32	33.9	7	38.8	2	33.3	32	34.7
Sterile in marriage	16	23.5			1	16.6	17	18.4
Natural menopause	33	48.5	3	16.6	1	16.6		
Surgical menopause	5	7.3	2	11.1				
Symptoms after menopause	27	39.7	1	5.5			28	30.4

ADDITIONAL DATA ON MENOPAUSE

	Adenocarcinoma Years	Carcinoma Years	Embryoma Years
Natural menopause			
Average age	47.6	44.6	45
Oldest age	58	53	45
Youngest	33	36	45
Surgical menopause			
Average age	42.4	44.5	..
Oldest	49	44	..
Youngest	39	39	..
Symptoms after			
Menopause average	8.7	1	..
Longest interval	20	1	..
Shortest mos.	1	1	..

TABLE III.—SYMPTOMS

	Adenocarcinoma		Carcinoma		Embryoma		Total	
Symptoms	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Pain in abdomen	38	55.8	14	77.7	5	83.3	57	61.9
Enlarged abdomen	30	44.1	5	27.7	1	16.6	36	39.1
Nausea and emesis	7	10.2	4	22.2	2	33.3	13	14.1
Backache	13	19.1	6	33.3	3	50.0	22	22.8
Headache			2	11.1	1	16.6	3	32.6
Loss of weight	12	17.6	2	11.1			14	15.2
Pain in rectum			1	5.5			1	1.08
Blood from rectum	2	2.9	1	5.5			3	3.26
Urinary disturbance, frequency, pain	10	14.7	4	22.2			14	15.2
Constipation	2	2.9					2	2.17
Gain in weight	2	2.9					2	2.17
Irregular menstrual periods	11	16.1	1	5.5			12	13.0
Pain on menstruating	2	2.9					2	2.17
Amenorrhea (recent)	2	2.9					2	2.17
Never menstruated					1	16.6	1	1.08
Vaginal bleeding	12	17.6	5	27.7			17	18.4
Leucorrhea	19	27.6	5	27.7	2	33.3	26	28.2
Miscarriage or abortion	16	23.5	3	16.6	1	16.6	20	21.7
Stillbirths			2	11.1			2	2.17

tial point in favor of malignancy in an ovarian tumor.

Menstrual disturbances, such as irregular periods, profuse flow, and pain were not present in the embryoma group although 2 of the 6 cases had a leucorrhea previous to admission. Menstrual irregularities for variable lengths of time previous to admission were noted in 16.1 per cent of the adenocarcinoma cases and 5.5 per cent of the carcinoma cases. Two of the adenocarcinoma group had quite severe pain on menstruating since the onset of their disease. Vaginal bleeding between periods but usually following menopause was present in 17.6 per cent of the adenocarcinoma cases and 27.7 per cent of the carcinoma group. It has been noted by other observers (Schroeder, Tietze) that in cases of ovarian malignancy a hyperplasia of the endometrium often takes place. This is especially true of the granulosa cell carcinomas. E. S. J. King explains this hyperplasia and also endometriosis by a hormonal action. He says: "It is possible that tumors consisting of cells which are closely allied to the granulosa cells—and therefore are presumably capable of producing the follicular hormone—which may be abnormal, either in amount or quality—may have a considerable effect on the endothelium e.g., overgrowth. . . . It has been shown that em-

TABLE IV.—AGE MENSTRUATION BEGAN

	Adenocarcinoma 68 cases	Carcinoma 18 cases	Embryoma 6 cases	Total	Per cent
Age in years					
11	4	2	0	6	6.52
12	14	3	1	18	19.5
13	21	3	2	26	28.2
14	12	5	2	19	20.6
15	8	2	1	11	11.9
16	9	1	0	10	10.8
17	2	1	0	3	3.26
18	0	2	0	2	2.17
Average age	13.9	14.7	13.5	14	.....
Youngest	11	11	13	11	.....
Oldest	17	18	15	18	.....

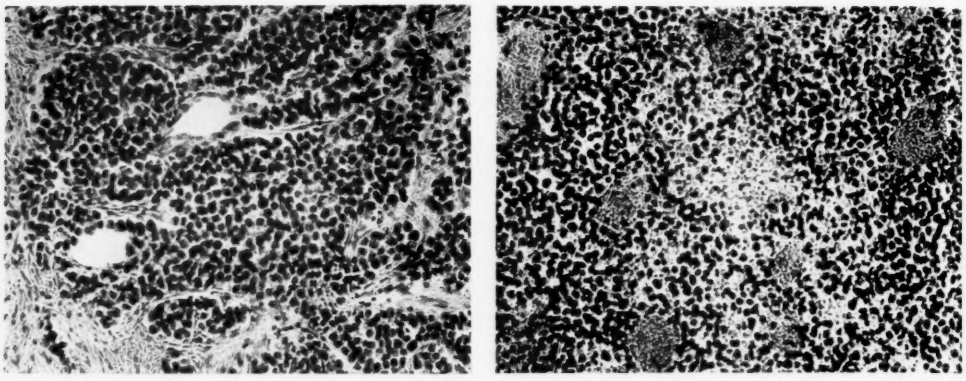

Fig. 8. Granulosa cell carcinoma. A, left, Masses of regular, round, somewhat clear cells tending to group in cylinders and about pseudo-alveoli; B, cells arranged about blood spaces. Case 17986; age, 23 years; single, nullipara; alive 4½ years after right ovarian tumor was removed (granulosa cell tumor), 2½ years after left ovarian tumor was removed (granulosa cell carcinoma), 1½ years after irradiation was begun.

bryonic tissue contains the hormone so therefore anaplastic type cells must contain an additional amount."

Novak reported a case in which after removal of a granulosa cell tumor the patient complained of a "second menopause" due to cessation of folliculin secretion. He says that this clinical syndrome has been described in only one other case (Schulze's case).

One of our granulosa cell carcinoma cases gave a history of periodic uterine bleeding beginning 1 year after a normal menopause. She was admitted to the Institute in a moribund condition and died in 6 days after receiving one X-ray treatment. Autopsy revealed an extensive tumor involving both ovarian regions and extending to the umbilicus.

Two adenocarcinoma patients had never had a menstrual flow due to age at onset of tumor growth.

Physical examination may not reveal the true character of the lesion. A palpably free mass, or a so called frozen pelvis with ascites and diffuse abdominal enlargement may be present. Even after metastasis has taken place, a malignant tumor may remain movable if pedunculated (Ewing). Many times pelvic examination affords little information as to which ovary is involved as either may be displaced.

On operation it was found that 72.47 per cent of the cases had growths in both ovaries. Shaw reported 76.7 per cent bilateral involvement and said: "If bilateral ovarian tumors are found at operation, the chances are nearly 5 to 1 in favor of the tumors being malignant."

One rarely sees distant metastasis in ovarian cancer, because the majority of these tumors spread by implantation. Four adenocarcinomas and 1 embryoma showed distant metastases. Shaw's observation that one may not find evidence of metastasis in cases of bilateral malignant tumors and that they may arise independently of one another seems logically true. Ewing states: "The majority of carcinomas are originally bilateral or soon become so."

The percentages of bilateral involvement of the cases in this series at operation are:

	Per cent
Adenocarcinoma	80.9
Carcinoma	55.5
Embryoma	33.3

TREATMENT

The judicial use of a combination of surgery and irradiation remains the best method in the treatment of malignant neoplasms of the ovary. With the knowledge that an ovarian tumor is malignant at the time of operation, it is justifiable to remove the other ovary, uterus, tubes, and broad ligaments, even though these structures are apparently normal in appearance and the patient is in the reproductive period of life. When widespread

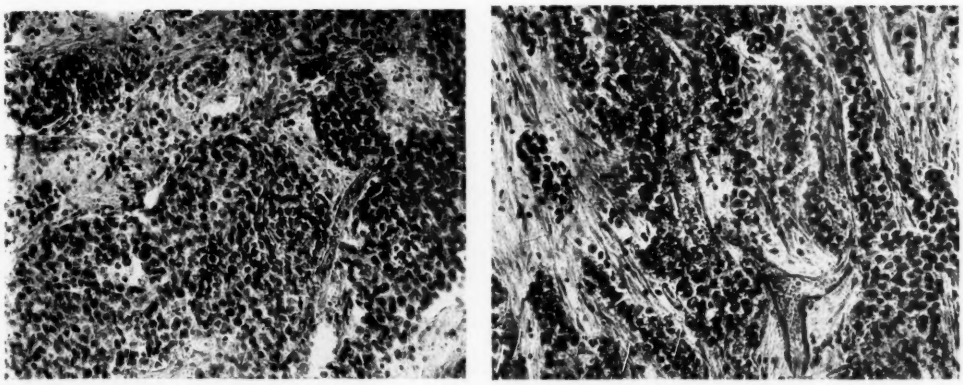

Fig. 9. Granulosa cell carcinoma. A, left, Groups of cells in loose formation; B, masses of cells in cylindrical formation and about blood spaces. Case 8147; age, 41 years; single; nullipara; died 9 years after palliation operation for ovarian tumors and irradiation (cause of death—cerebral hemorrhage); very radiosensitive.

metastasis is present Keene, Pancoast, and Pendergrass have found in unusual cases "rather marked improvement in general health and retardation of the malignant process" by excision alone of the primary growth. Since any such case in our series has been irradiated following operation, improvement, when noted, was credited to the radiation therapy. It is apparent that many of these metastatic cases, even when only a diagnostic laparotomy has been performed, show a marked palliation of symptoms and prolongation of life following treatment by irradiation therapy.

In discussing the value of irradiation in the treatment of ovarian tumors, it is essential to know the type and extension of the neoplasm. Morphologically similar tumors may show a difference in their response to radiation therapy. It is apparent that there exists an individual variation in the reaction of the tissue bed to irradiation.

Irradiation treatment in this Institute was carried out by means of X-ray and radium, separately, or in combination.

X-ray. Prior to 1921 medium voltage X-ray with aluminum filter was used. Three of the adenocarcinoma cases and one of the embryoma cases were treated in this manner. It is apparent now that the doses which were used at that time were inadequate. Since 1921 high voltage X-ray therapy has been used. The factors are:

Volts	200,000
Milliamperes	30
Distance	80 centimeters
Angle	90 degree
Field size	20 by 25 centimeters
Filter—copper	.5 millimeter
aluminum	1.0 millimeter

The tumor dose was computed from the patient's pelvic measurement by means of isodose charts. Cross fire was accomplished through two portals—anterior and posterior—in divided amounts sufficient to produce a skin erythema dose, which in this Institute represents 800 roentgens (air scattering) and 1130 roentgens (tissue scattering). The course was usually repeated in 2 months if the patient's condition warranted. As many as 6 courses have been given within a period of 3 years. Occasionally more than two fields were used.

Radium packs. Radium packs prior to 1931 were used at 6 centimeters' distance with a filter of 2 millimeters of brass, 0.5 millimeter of silver, 1 millimeter of aluminum, and 1 centimeter of rubber.

The size of field was 6.5 by 7.5 centimeters through 2 or 3 portals, anterior and posterior, and sometimes perineal. Doses were as high as 26,420 milligram hours in one course.

Since 1931 the 4 gram radium element pack has been used. When two fields—anterior and posterior—were used at 10 centimeters' distance, dimensions of field size were 20.5 by 20.5 centimeters. Occasionally two anterior,

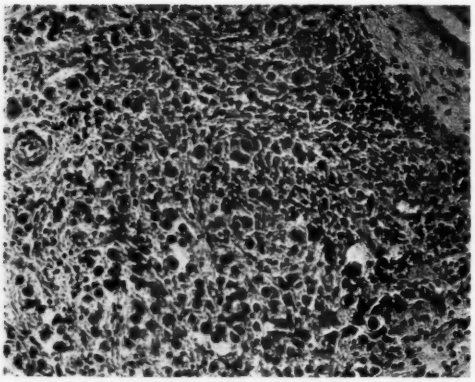

Fig. 10. Granulosa cell carcinoma. More "unripe" type with some lymphoid stroma. Case 9824; age, 11 years; single; nullipara; died 16 months after left ovarian tumor was removed and 13 months after irradiation was begun.

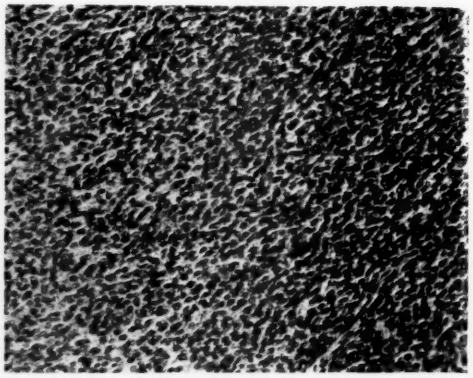

Fig. 11. Embryonal cell carcinoma. Case 11361; age, 41 years; married; multipara 4; died 3 years after an operation for the removal of an unilateral ovarian tumor was performed and treatment by irradiation therapy was instituted.

two posterior, and one perineal field were used at 10 centimeters' distance. Here the field size was 10 by 10 centimeters. Filter was 1 millimeter of platinum, 1.5 millimeter of steel with a secondary filter next to the skin of 0.5 millimeter of copper, and 1.0 millimeter of aluminum. The dose has been as high as 705,000 milligram hours given in 5 courses of 10 treatments each, alternating anterior and posterior over a period of 9 months.

Intracavitary. Before 1931 radium emanation was used in two 50 millicurie tubes placed in tandem into cervix uteri. Dose varied from 1200 to 2400 millicurie hours. Filter was 0.5 millimeter gold, 0.5 millimeter brass, and 1.0 millimeter rubber. Since 1931 radium element has been used in a 100 milligram tube. Filter 1.0 millimeter platinum and 1.0 millimeter aluminum. Dose from 1200 to 2400 milligram hours.

Nine cases received this type of therapy in conjunction with radium pack or X-ray therapy.

Interstitial. In a few cases radon seeds were placed in the cervix uteri for local conditions of the cervix at the time diagnostic curettage or biopsy of cervix was done. This was always in conjunction with external irradiation.

Two of the cases received pre-operative irradiation only, due to the advanced condition of envolvement. One was an adenocarcinoma and the other an alveolar carcinoma. One embryoma case received both pre-operative and postoperative irradiation.

RESULTS

It is very difficult to reach any positive or detailed conclusion as to end-results in cases of intra-abdominal malignancies. This is especially true for those tumors affecting the ovary since each case is an integral cancer study in itself. Not only do the tumors of the same group differ in many pathological respects, but there is a great variation in the duration of the growth before the first symptoms are noticed. Any predisposing factor, such as a benign neoplasm or a fetal inclusion, may obscure the clinical history before a diagnosis is made. Even surgical intervention is not always adequate in those cases in which complete extirpation of the tumor is recorded. The radiosensitivity of the malignant cells is no more important than the reactionary power of the host to the irradiation. It is apparent that all these factors enter into any discussion of results which are measured according to length of life not only following complete or incomplete operation but also following treatment by irradiation.

According to these two headings the three main case groups have been divided into those who are alive or dead following complete or

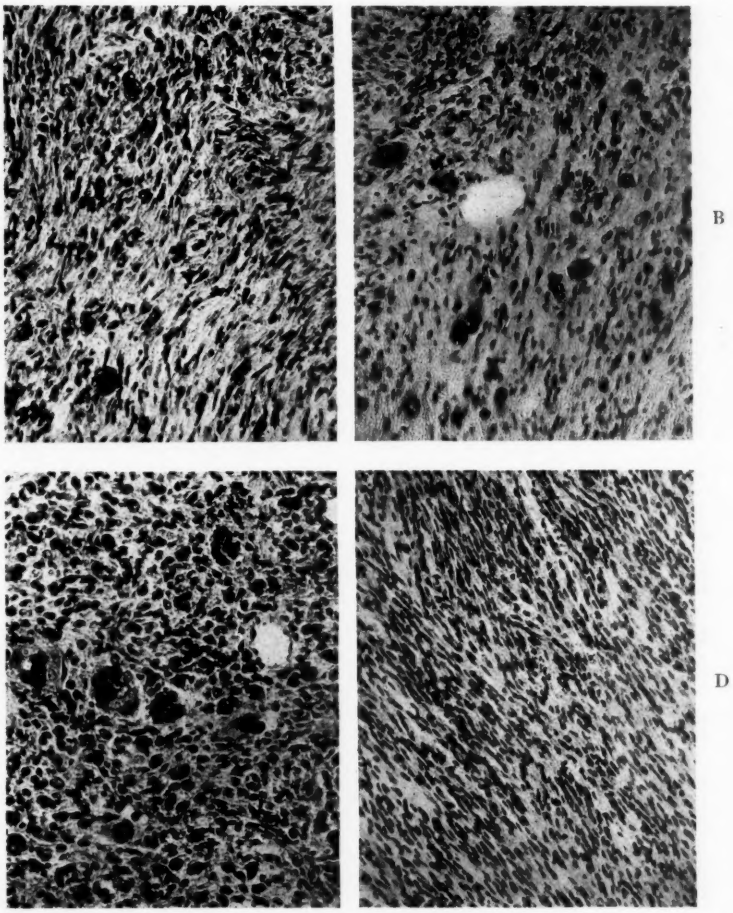

Fig. 12. Malignant embryoma. Shows giant cells, epithelium-like cells, and spindle cells in variety of stroma. Case 6402; age, 38 years; married; multipara 3; died 1 year, 8 months after removal of unilateral ovarian tumor and 1 year, 7 months after irradiation was begun.

palliative (or diagnostic) operations. Notice was made as to whether the growth at operation was bilateral or unilateral (Table V). In most cases treatment was begun soon after operation. There are 3 cases, however, in which irradiation was given before the abdomen was opened for pathological examination. This was due to the fact that the clinical evidence was strongly in favor of extensive malignancy. This accounts for the longer length of life period in those cases following treatment than the same cases following operation. The end-results for those cases in which complete operation was performed are much better than those in which only palliation was accomplished. Of course this latter group came to the surgeon much too late, but some effort may be made at appraising the irradiation effect.

In comparing the three main groups, it is found that the adenocarcinoma cases have not only a longer average life period following operation and treatment but also present the longest case survival—10 years. But the per-

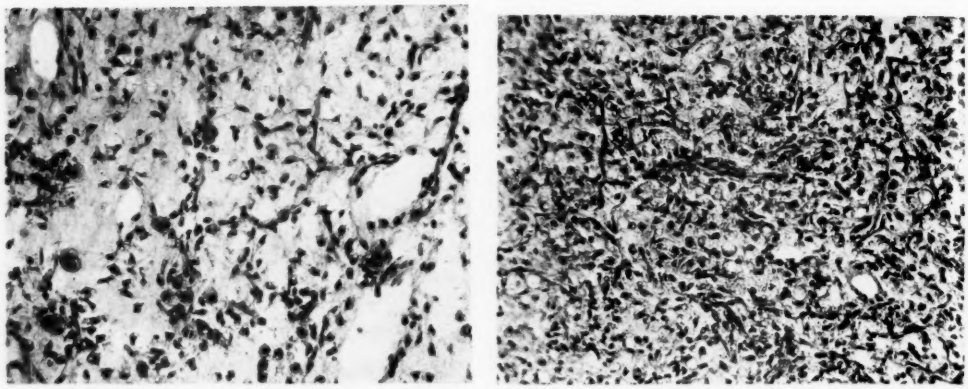

Fig. 13. Malignant embryoma. A, left, Shows myxosarcoma with giant cells; B, shows spindle cells and signet cells with mucoid stroma. Case 11780; age, 34 years; married; multipara 4.

centage of the patients who are alive is only 18.8. This may be explained by the clinical fact that late recurrences are the rule and not the exception (Thibaudeau), thus cutting down the percentage of live cases while the duration of life is increased. This does not compare favorably with the corresponding percentage in the carcinoma group (50 per cent).

The following chart shows not only this, but also the percentage alive and without evidence of recurrence.

Group	Cases	Alive		Alive and without recurrence	
		No.	Per cent	No.	Per cent alive
Adenocarcinoma	68	13	18.8	5	38.4
Carcinoma	18	9	50.0	3	33.3
Embryoma	6	0	0	0	0

In analyzing the several groups, we attempted to correlate the histological findings with the end-results of operation and irradiation.

Adenocarcinoma. The longest case survivals were those in which complete removal of the tumor was accomplished and in which the histological section showed a low grade of papillary adenocarcinoma with psammoma bodies (Fig. 15). Of the 13 patients who lived 3 years or longer following operation and treatment, 6 were of this type.

There are, however, cases in which a pronounced malignant picture is present and still the patient survives over the 3 year period. This is especially true for those types in which widespread involvement has not yet taken place. The large doses of radiation which these cases had certainly were factors in prolonging life.

Many patients come to operation too late (Fig. 16). In these patients only palliation or diagnostic procedures were attempted. Ample clinical evidence is obtained in this group in respect to the radioresistance of most ovarian adenocarcinoma cases.

Even in the case of a well formed adenocarcinomatous structure, in which the tumor is apparently adequately removed, one may see irradiation to be of little effect in preventing recurrences.

It is apparent that there is no positive criterion in prophesying the prognosis. The more malignant types tend to be further advanced at time of operation, and in many cases in which a complete removal of a unilateral ovarian tumor is recorded extension to the other ovary may already have taken place without its gross alteration. Or else, tumor cells remain in the mesovarian or broad ligament. It may be that those patients who survived the longer periods were more sensitive as hosts to the irradiation treatment. The gross and histological characteristics do not offer any basis for determining the relative radiosensitivity of these tumors. It is safe to say that early operation in which complete

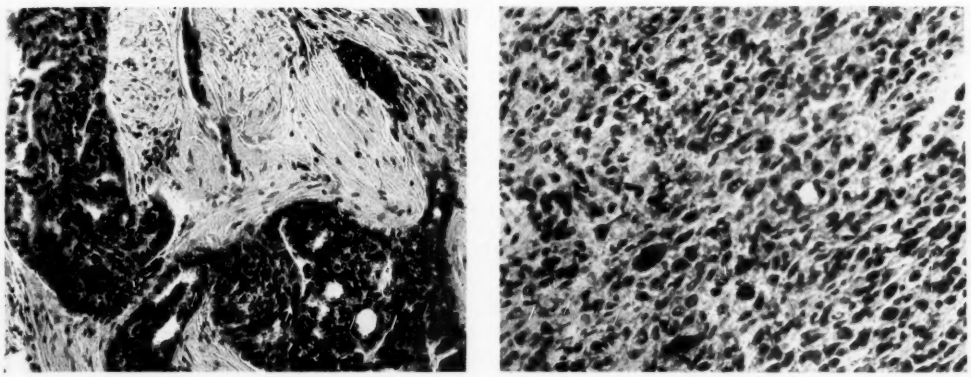

Fig. 14. Malignant embryoma. A, left, Shows adenocarcinoma of ovary found at operation; B, shows embryoma of ovary found at autopsy. Case 13398; age, 33 years; married; multipara 6; died 3 years after irradiation was begun and 2 years, 10 months after bilateral ovarian tumors were removed.

excision of both ovaries is possible and full tumor doses of irradiation remain the best methods of treatment.

Carcinoma. Since the tumors differ widely in their pathological characteristics, each subgroup will be considered separately.

1. *Medullary type.* Of the 4 cases recorded only one is alive and apparently without signs of recurrence. The average length of life for those who are dead is 1.2 years, the longest and shortest being 2 years and 5 months, respectively. The former case died of chronic nephritis while the latter appeared too far advanced to discredit radiation treatment. A third case which survived for 1 year after treatment had a carcinomatous tumor showing mucoid degeneration (Fig. 6). Of course, this was radioresistant. The surviving case had bilateral tumors removed and has received 1423 r (tissue scattering). An adequate surgical removal plus this irradiation has so far kept the patient free from recurrence for $3\frac{1}{2}$ years.

2. *Alveolar type.* One case is alive and apparently without recurrence for 10 months. The 3 other patients are dead. The length of life averaged about 7 months, the longest being 1 year (Fig. 7) and the shortest 4 months.

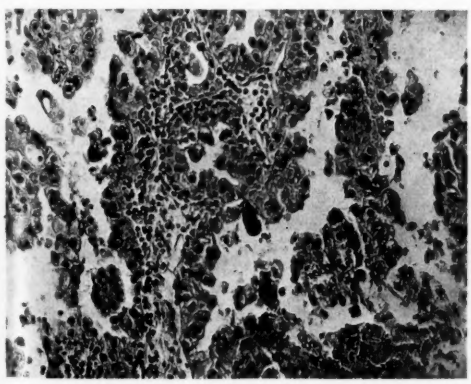

Fig. 15. Papillary cyst adenocarcinoma of low grade malignancy. Shows psammoma bodies. Case 12494; age, 48 years; married; multipara 2; alive and without evident recurrence 4 years, 8 months after irradiation and 5 years, 2 months after removal of a unilateral ovarian tumor.

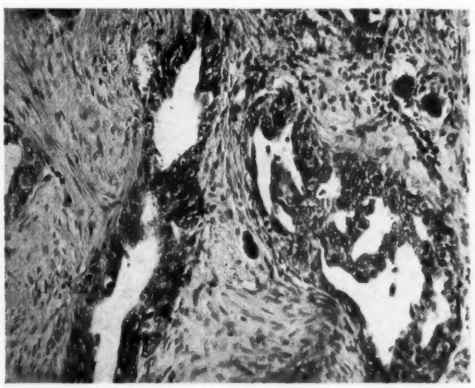

Fig. 16. Adenocarcinoma. Very malignant with widespread metastasis. Case 12946; age, 50 years; married; nullipara; died 2 months after a diagnostic alparotomy had been performed and irradiation therapy had been instituted.

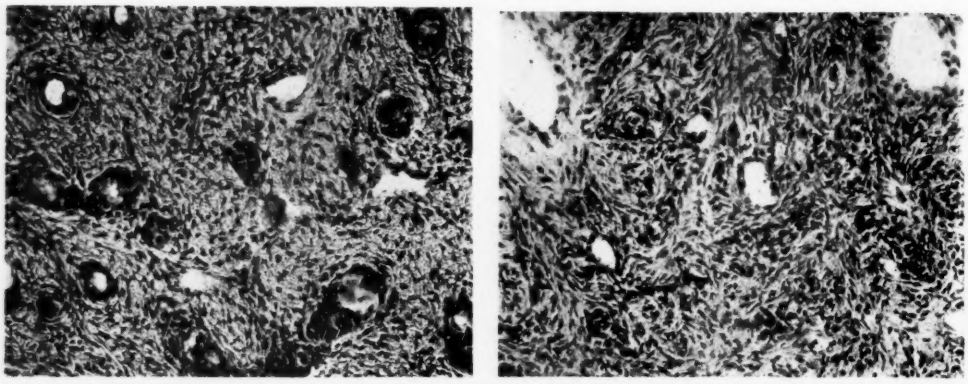

Fig. 17. Granulosa cell carcinoma. Resembles in some respects oophoroma folliculare. Case 15918; age, 42 years; married; multipara 2; died 6 months after an operation for the removal of an unilateral ovarian tumor and 4 months after irradiation had been instituted.

In all these cases the cells were of a marked malignant quality. Their response to irradiation was poor. The 1 case alive, in which bilateral ovarian tumors were removed, has felt well. She has received 210,000 milligram hours of radium pack. It may be that surgery was adequate. The microscopical structure of the tumor showed radiosensitive qualities. It is too early to appraise any results in this case.

3. *Granulosa cell type.* Three cases are alive and without evidence of recurrence for the following lengths of time after treatment was begun, one for 3 years and two for 1½ years. Both of the latter 2 cases are interesting in showing late recurrence. Four cases are dead —lengths of life being 9 years (died from cerebral hemorrhage), 4 months, 13 months, 6 days after treatment was begun following operation. The first case (Fig. 9) had a palliative operation which was followed by three courses of radium pack which were given over a period of 3 years and two courses of deep X-ray therapy.

TABLE V, A.—POSTOPERATIVE. LENGTH OF LIFE

Group	Alive or dead	Unilateral or bilateral	Removal of tumor							Palliative or diagnostic						
			No.	Average		Longest		Shortest		No.	Average		Longest		Shortest	
				yr.	mo.	yr.	mo.	yr.	mo.		yr.	mo.	yr.	mo.	yr.	mo.
Adenocarcinoma	Alive	U	4	4		4	6	2	6							
		B	9	3	6	10			2							
	Dead	U	8	2	6	7			6	1	3		3		3	
		B	22	2	4	5	4		3	24		11	6			2 days
Carcinoma	Alive	U	5	2	6	3	6	2	2							
		B	4	1	11	3	8		8							
	Dead	U	3	1	1	1	6		6							
		B	1	3		3		3		5	2	2	9			1
Embryoma	Alive	U														
		B														
	Dead	U	3	1		1	8		6	1	2	6	2	6	2	6
		B	1	2	10	2	10	2	10	1		5		5		5

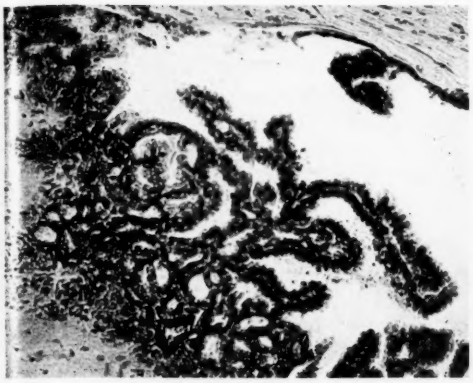

Fig. 18. Papillary cystadenocarcinoma. Shows malignant structure in wall of cystic tumor. Case 7473; age, 29 years; married; primipara; died 5 years, 10 months after removal of a unilateral ovarian tumor and 5 years, 11 months after irradiation treatment was started.

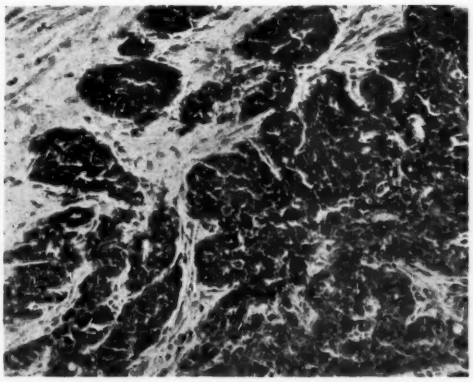

Fig. 19. Adenocarcinoma. Shows moderately well formed adenocarcinomatous formations. Case 12377; age, 39 years; married; nullipara; died 3 years, 4 months after bilateral ovariectomy and 3 years after irradiation was begun.

The second case did not respond to irradiation. It does not present the typical granulosa cell carcinoma picture and has a great amount of dense stroma (Fig. 17). In some respects, it resembles the oophoroma folliculare type of tumor. This patient died 4 months after a total of 1152 r (tissue scattering) in 4 treatments in 8 days was given over pelvis for a large tumor mass in the posterior cul-de-sac.

The third case, an 11 year old girl with an unripe granulosa cell carcinoma (Fig. 10) after a diagnostic operation received a total of 2576 r (tissue scattering) in two courses 7 months apart. She died 13 months after admittance. X-ray, although not curing this girl, proved very palliative and no doubt was responsible for prolonging her life.

The fourth patient was admitted in an almost moribund condition and after receiving one X-ray treatment (565 r tissue scattering) died in 6 days. Autopsy revealed a large tumor mass in the pelvis extending to the umbilicus. Section proved the growth to be a granulosa cell carcinoma.

TABLE V, B.—POSTADMISSION (TREATMENT). LENGTH OF LIFE

Group	Alive or dead	Unilateral or bilateral	Removal of tumor							Palliative or diagnostic						
			No.	Average		Longest		Shortest		No.	Average		Longest		Shortest	
				yr.	mo.	yr.	mo.	yr.	mo.		yr.	mo.	yr.	mo.	yr.	mo.
Adenocarcinoma	Alive	U	4	3	6	3	6	2	6							
		B	9	3		2	6		2							
	Dead	U	8	1	1	2	6		2	1	2	8	2	8	2	8
		B	22		10	3			2	24		9	6			2 days
Carcinoma	Alive	U	5	2	6	2	10	1								
		B	4		8		10		6							
	Dead	U	3		9	1	1		4							
		B	1	3		3		3		5	2	7	9			4
Embryoma	Alive	U														
		B														
	Dead	U	3	1		1	6		6	1		2		2		2
		B	1	3		3		3		1		4		4		4

4. *Embryonal cell type.* This is a comparatively radiosensitive tumor. Stewart has stated that "massive regression may be expected, but massive recurrence with gradually increasing resistance has occurred." At the Memorial Hospital, this class of case had not been successfully controlled. We have only 3 cases. Two are alive and without evidence of recurrence; 1 for 2½ years and the other for 1½ years. The 1 who is dead lived for 3 years after X-ray therapy was begun (Fig. 11). She died from bowel obstruction.

From these few carcinoma cases, it is not possible to draw any definite conclusions as to radiosensitivity. It may be stated, however, that the embryonal carcinoma and the granulosa cell carcinoma are more radiosensitive than the medullary and alveolar types. Also, since recurrence is common, even after a so called complete extirpation of a tumor, irradiation is indicated. The tumors vary as to their response to this irradiation. The granulosa cell carcinomas, when of a more "ripe" character, offer more possibilities for cure from surgery and irradiation than the unripe types.

Embryoma. Every one of the embryoma cases presented a different histological picture. All the patients are dead. One patient lived 3 years after admission and 2 years, 10 months, after operation. The average length of life for all the others was less than 1 year, the longest being 18 months and the shortest 2 months. In none could one determine what the outcome might be from the gross or histological envolvement. As is true for all malignant embryomas, one type of cell may predominate, although in all of our cases a combination of cellular forms was present. This makes the estimation of radiosensitivity rather hard.

CONCLUSIONS

1. Primary malignant neoplasms of the ovary present a complex study due to the differences in research data regarding its embryology and histological transformations.

2. Most ovarian malignancies arise from germinal epithelium or from benign germinal epithelial tumors through malignant degeneration. Others arise from embryonic rests and ovulogenic neoplasms.

3. A division into three main groups and a pathological description of each type have been made.

4. From a survey of the literature and our own cases it is found that ovarian cancer is not uncommon and that no age is excepted. The greatest number occur between 30 and 60 years of age. Our extremes were 11 and 69 years of age.

5. In our cases 73.9 per cent were married; 55.4 per cent had been pregnant from one to ten times, the average being from two to four; 21.7 per cent had miscarriages or abortions; 23.5 per cent of the adenocarcinoma cases and 16.6 per cent of the embryoma cases were sterile in marriage; 39.7 per cent of the adenocarcinoma cases and one granulosa cell carcinoma had passed an apparently normal menopause when first symptoms occurred. These figures testify for the hormonal functional association in the etiology of ovarian cancer, both in the normal and abnormal capacity.

6. Pre-diagnostic length of symptoms average from 11 to 15 months. They are most severe in the carcinoma group. Pain in the abdomen and enlargement of the abdomen are the outstanding complaints in all groups. The clinical picture is discussed with special reference to endocrinological syndromes of the granulosa cell carcinoma.

7. Results are judged according to length of life following complete or palliative operation for unilateral or bilateral tumors, and also following irradiation.

8. Best average results were in the adenocarcinoma group, probably due to a number of early low grade malignant cases which furnished better surgical material.

The embryoma group yielded the worst end-results.

Of the carcinoma group, the alveolar type showed the poorest results. The granulosa cell and embryomal cell types were most favorable.

In all groups complete removal of tumors gave longer survivals than palliative procedures.

9. Differences in radiosensitivity are found. The host's reaction to irradiation is important.

The granulosa cell and embryonal cell types

of carcinoma are most sensitive. Both tend to recur.

The low grade malignant type of adenocarcinomas offer the best results from surgery and irradiation in this pathological group. Other adenocarcinomas tend to be radioresistant, as do the alveolar and medullary carcinomas found in this series.

10. Treatment to be adequate must consist of early surgical removal of both ovaries, followed by deep irradiation in large tumor doses.

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HYPOPLASIA OF THE KIDNEY[1]

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THE difficulties encountered in attempts to decipher the pathological alterations and embryological defects of kidneys of the type usually classified as rudimentary, hypoplastic, or aplastic kidneys, are probably directly related to the confusion that exists in the literature on hypoplasia of the kidney. Congenital atrophy, aplasia, agenesis, rudimentary and infantile kidney are names used and, not infrequently, without strict adherence to the pathological definitions of hypoplasia, aplasia, and acquired disease.

At the present time, it seems best to separate these kidneys into two main groups. One group would include all kidneys altered by acquired diseases such as inflammation, circulatory disturbances, trauma, and hydronephrotic obstruction. Regardless of the time such changes occur, whether in fetal or postfetal life, the name should include the concept of acquired atrophy. The other group would comprise all kidneys altered because of hypoplasia or aplasia of the metanephric mass, the derivatives of the primary excretory duct or those of the vascular elements. Hypoplasia would be used when there is a diminution in size due to decrease of the number of cellular elements or decrease in the size of the cells or both. Aplasia would be properly used when there are no remnants of these original structures.

Fig. 1. Case 1. Retrograde pyelogram, demonstrating an elongated, rudimentary right renal pelvis with an upper protruding superior calyx.

It is usually difficult to separate acquired atrophic kidneys from the hypoplastic or the aplastic kidneys because subsequent disturbances from inflammation, from circulatory disturbances, or from hydronephrotic obstruction frequently alter the latter type. For this reason, histological standards for differentiating the two should be emphasized so that a more definite basis for diagnosis is made available.

The three renal malformations described herein seem to offer good criteria for some of these differentiations. In the first instance, aplasia of the elements derived from the metanephric mass best explains the characteristics of the kidney. In the second instance, bilateral complete hypoplasia of all of the elements derived from the primary excretory duct offers a satisfactory interpretation of the alterations. In the third instance, the changes are limited to the superior calyx of the kidney, and here also hypoplasia of part of the elements derived from the excretory duct is most consistent with the essential features of this pathological malformation.

The clinical diagnosis of the congenital hypoplastic kidney is often difficult and of considerable importance in renal surgery because it alone will not sustain life and, not infrequently, due to acquired disease, is a source of danger to the other kidney.

Hypoplasia of the kidney was known to Blasius in 1677. Ballowitz (1895) assembled 20 cases, Risel (1903) 36 cases. Since that time many cases have been added to the literature, some of which are definitely hypoplastic, whereas others should be classified as acquired atrophy or one of the other forms of congenital anomaly.

According to Papin, hypoplastic kidneys are more frequently found in men than women, and the right side is more often

[1] Read at the First Meeting of the Southeastern Branch of the American Urological Association, Atlanta, Georgia, December 7 and 8, 1934

affected. It has been found in all ages, from the fetus to advanced life. In the living, it is always unilateral since if bilateral, it could not sustain life. It may lie in a normal position or may be ectopic. The renal pelvis is usually small and frequently cone shaped with small calyces, some of which may be rudimentary in type.

The ureter is often small, and may even be obliterated. In some cases it is normal, dilated, anomalous, or entirely absent. The vessels of the renal pedicle are small in many instances, but at times normal in appearance, in others obliterated or absent.

As a rule the opposite kidney is hypertrophied, but in some cases it may appear to be normal or smaller in size. Associated anomalies of the genito-urinary tract are not infrequent findings.

The embryological arrest that causes renal hypoplasia may involve the nephrogenic tissue, the wolffian duct, or both (Papin). The symptoms may be few and difficult to interpret, reduction or absence of function being the only sign. The symptoms may be referred to the opposite side. The signs and symptoms of almost any renal disease may be found in these cases. The diagnosis is often difficult. The roentgenological examination may show one large and one small kidney. The pyelogram may visualize a rudimentary type of pelvis. The cystoscopic examination may show changes in the trigone and the ureteral orifices which may be helpful in making the diagnosis.

The functional test is of value in that the function of the affected side is reduced or wanting. The opposite kidney, which is usually the seat of compensatory hypertrophy, must bear the entire excretory burden and, from a surgical standpoint, must be considered a solitary kidney.

Fig. 2. Case 1. Right kidney, illustrating marked atrophy of the parenchyma and a renal pelvis that is elongated and altered by extensive hyperplasia of lymphoid tissue.

Case 1. A woman, aged 28 years, on admission to the hospital, stated that she had suffered from cystitis since childhood. These attacks were intermittent and often ushered in with chills and fever, frequency, and urgency. She had been treated with various forms of medication which gave only temporary relief. She had always been underweight, and had been unable to overcome this after making many efforts. She had pain in both flanks which varied in intensity and was more often felt on the right side. Pus was found in the urine on many occasions and she thought her urine always contained some pus. She had never had any hematuria.

Physical examination disclosed a tall, thin, pale woman who did not appear acutely ill but showed the effect of long standing invalidism. The catheterized bladder urine contained many pus cells and on culture showed Bacillus coli.

Fig. 3. Case 1. Photomicrograph through the parenchyma from the capsule to the hilus. Active glomeruli or remnants of glomeruli are not observed. Tubular spaces, most of them without a cellular lining, are the only structures present.

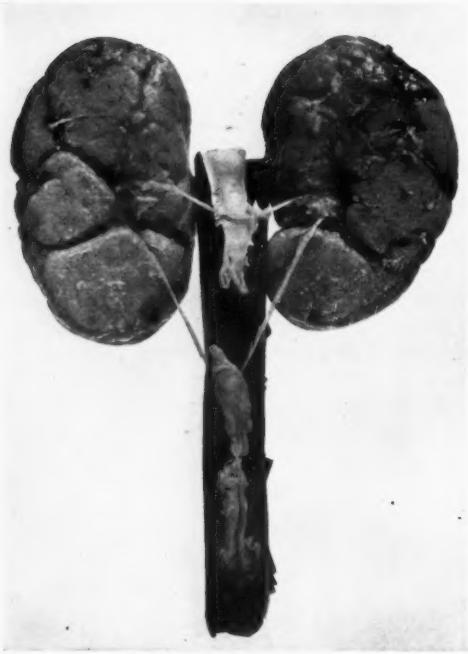

Fig. 4. Case 2. Urinary tract from newly born infant with large, cystic kidneys, hypoplastic ureters and renal pelvis, and epispadias.

Cystoscopic examination revealed marked hyperemia of the bladder mucosa, especially in the region of the trigone. The right ureteral orifice was round and somewhat retracted, the left was normal. A catheterized specimen from the right kidney was very small in quantity (2 to 4 c.cm), contained

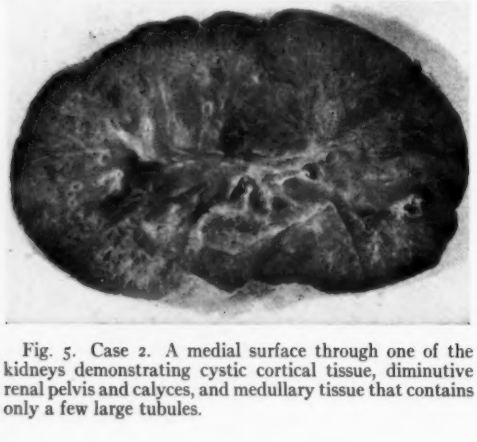

Fig. 5. Case 2. A medial surface through one of the kidneys demonstrating cystic cortical tissue, diminutive renal pelvis and calyces, and medullary tissue that contains only a few large tubules.

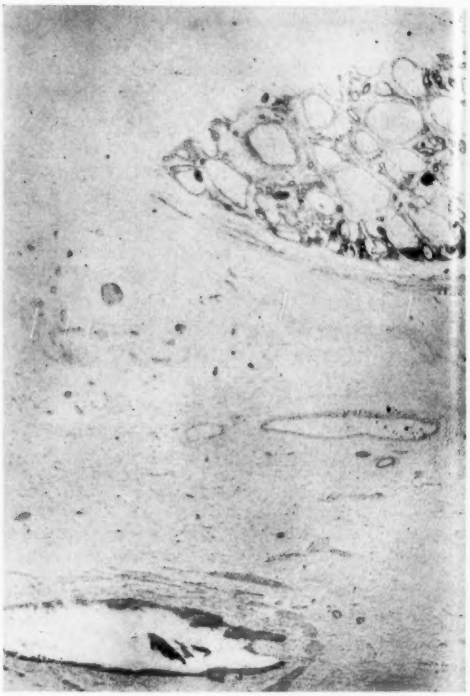

Fig. 6. Case 2. Photomicrograph illustrating a moderately mature cortex with dilated glomerular spaces, a minor calyx, and the medulla in which there are only a few collecting tubules, the larger ones possessing transitional epithelium.

many pus cells and on culture showed Bacillus coli. Left kidney secretion was normal in amount, low cell count, and sterile. All urines were negative for tubercle bacilli, both in smears and guinea pig inoculations. There was no excretion of phenolsulphonphthalein from the right kidney and a normal amount from the left following intravenous injection of the dye.

The blood chemistry was normal. The blood count showed a mild secondary anemia and white blood cells, 14,000. The retrograde pyelogram (Fig. 1) demonstrated a rudimentary type of pelvis on the right side, the pelvis being markedly elongated, and only one small calyx was observed at the upper end. The left pyelogram was normal.

After prolonged local treatment, the patient finally consented to a right nephrectomy. The kidney was difficult to find because of its small size. Extending inferiorly from it was found a long cone shaped pelvis.

Gross pathology. The right kidney (Fig. 2) had a maximum length of 5 centimeters, and maximum width of 2.5. It was shaped like a normal kidney

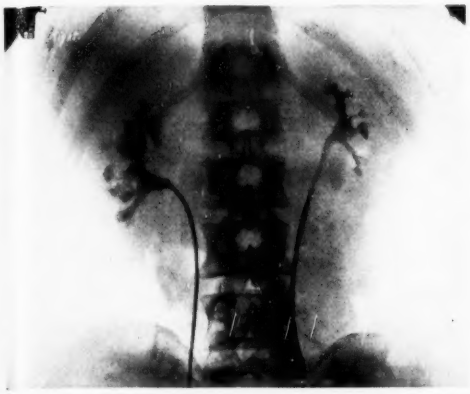

Fig. 7. Case 3. Roentgenogram of right kidney illustrating a destructive lesion of the middle and upper calyces.

except for the renal pelvis which was large in proportion to the kidney mass, and which, when opened, had a pyramidal shape. There were two major calyces, each being rounded and connected with the renal pelvis through an opening smaller than the greatest diameter of the calyx. The wall of the renal pelvis and calyces was thrown into convoluted, parallel folds, 2 to 3 millimeters wide, pigmented brown, and their lining smooth. No distinct medullary pyramids were observed, the entire mass of renal parenchyma being formed of light brown tissue, 4 to 5 millimeters wide. There were no striations like those of the normal medulla and cortex. The capsule was tightly adherent. There were no significant changes in the renal artery or vein.

The histological characteristics (Fig. 3) center about tubular spaces that occupy all of the parenchymal mass. Most of them are round, vary slightly in size, and the lumina of most are occupied by hyaline masses. These spaces have thin walls, lining cells not being present in the majority of tubules. In sections made from the upper to the lower pole, no structures are found that represent active or obliterated glomeruli. These tubules extend to the calyces.

In this kidney, the ureter, renal pelvis, and major calyces are developed to a size that is almost that of the normal kidney. In the kidney substance, only tubular structures are found. The essential derivatives of the metanephric mass, namely glomeruli, are not present. Usually when acquired lesions produce atrophy, remnants of the glomeruli are found. The conclusion reached concerning the pathogenesis of this kidney postulates that hypoplasia or aplasia of the metanephric mass occurred, whereas the derivatives of the primary excretory duct continued well on to mature development. The hyperplastic lymphoid tissue in the lining of the renal pelvis is probably related to chronic pyelitis.

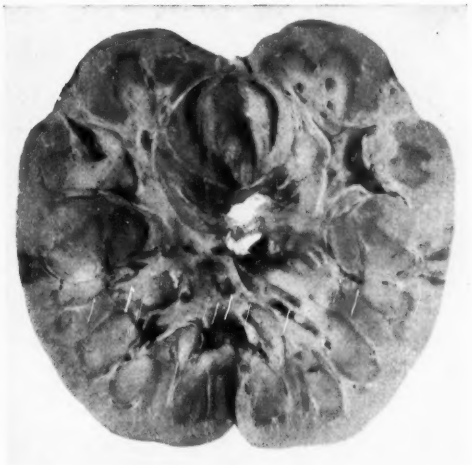

Fig. 8. Case 3. Right kidney illustrating a cyst at the upper pole, dilatation of the superior calyx and cysts in the medullary pyramids of the superior pole.

CASE 2. This urinary tract (Fig. 4) was found in a full term male child that lived 1 hour. There were two large, boggy kidneys, with irregularly developed fetal lobation markings, a short thin ureter on each side and the hilus displaced to the posterior surface of each kidney. In addition, there was a diminutive urinary bladder and an epispadias. In a surface through each kidney (Fig. 5), the outstanding changes were represented by a renal pelvis the circumference of which was no greater than that of the ureter, by two short calyces also of diminutive size, by medullary pyramids in which there was only edematous tissue with a few large tubules in them. The cortical portion of the kidney was swollen, wet and made up of numerous pinpoint to pinhead size cysts. There were three irregularly formed columns of Bertini.

Histologically, the cortex was characterized (Fig. 6) by dilated glomerular spaces, the glomerular tufts being approximately the size of those of a full term infant. These dilated glomerular spaces and convoluted tubules were separated by edematous stroma. A section through both cortex and medulla demonstrated a medulla in which there were only a few tubules, some of which had transitional epithelium like that of the renal pelvis instead of the normal single layer of cuboidal epithelium.

In this urinary tract, the cortical elements were developed to a fairly mature stage for a

Fig. 9. Photomicrograph of one of the medullary pyramids of the superior pole illustrating sparsity of collecting tubules and a few large tubules and cysts lined with transitional epithelium.

newly born infant, whereas in the medulla there are only isolated immature collecting tubules. The explanation of the gross and microscopic characteristics is based on hypoplasia of all of the elements that are derived from primary excretory duct, namely, part of the bladder, ureters, renal pelves, and collecting tubules, whereas the derivatives of the metanephric mass developed in a normal manner. The dilation of the glomerular spaces and convoluted tubules was due to an inadequate number of collecting tubules for excretion. The presence of epispadias is not connected directly with the malformation of the primary excretory duct, but is a concomitant malformation.

CASE 3. This patient, a physician aged 37 years, noticed blood in his urine. A cystoscopic examination was made the same day and blood was noted coming from the right ureter. There was some pain in the right flank following a retrograde pyelogram, but this disappeared in a few days. Other than this, the patient did not have any signs or symptoms directed to the urinary tract.

On admission to the hospital the cystoscopic examination failed to reveal any changes in the bladder except some reddening of the ureteral orifices resulting from previous catheterization.

Sterile urines were obtained from both right kidney and bladder and a study for tuberculosis was negative.

A retrograde pyelogram of right kidney (Fig. 7) showed kidney opposite the second lumbar vertebræ. Pelvis was of normal size. There appeared to be destruction of the middle and upper calyces extending beyond their limits into the kidney substance.

In view of the presence of hematuria and because of the changes seen in the pyelogram, the patient, being a medical man, came to the conclusion that he had a renal neoplasm and therefore requested that the kidney be removed.

Gross pathology. The alterations in this kidney (Fig. 8) were limited to the superior pole. There was a cyst 3 centimeters in diameter with a wall 2 to 3 millimeters thick, the lining composed of granular, gritty material. In addition, the medullary pyramids of the superior major calyx were changed by cysts of various sizes. Under the largest of these cysts, there were noticeable depressions in the surface of the kidney which were caused by atrophy of the cortex.

These alterations histologically at the upper pole (Fig. 9) were characterized by the presence of only a few collecting tubules in the medullary pyramids, some of which were dilated. The most important characteristic was the presence of a lining made up of transitional epithelium like that of the renal pelvis. Surrounding some of the tubules, there was a lymphocytic infiltration. In the lining of the superior calyx there were several large hemorrhages.

The explanation of the pathogenesis of these cysts rests on retardation in the development of the later generations of collecting tubules. There was a failure also of the usual unification of the collecting tubules of the third to the fifth generations. It seems more reasonable to explain the presence of a few tubules and transitional epithelium within the medullary pyramids on the basis of retarded development rather than on metaplasia and atrophy. The failure on the part of the collecting tubules to join properly with the renal pelvis undoubtedly accounts for the dilation and formation of cysts.

In former years there was a general tendency to explain cystic malformations of the kidneys on the basis of inflammation and subsequent occlusion of ducts. At the present

time, there is more frequent reference to developmental error as the probable etiological factor in the causation of cysts.

SUMMARY

The clinical alterations and the pathological characteristics are presented of three forms of renal change that are interpreted as resulting from hypoplasia or aplasia of specific portions of the early third kidney.

Histological characteristics are emphasized which seem to be standards that may be used in deciphering rudimentary kidneys resulting from retarded development of the derivatives of the primary excretory duct or of the metanephric mass.

The desirability of simplifying the terminology, until more exacting histological and embryological characteristics are established, is expressed.

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GENERALIZED HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

An Experimental and Clinical Study with Report of Two Cases

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CLUBBING of the fingers, swelling of the joints, and periosteal new bone formation secondary to intrathoracic lesions such as bronchiectasis, empyema, lung abscess, bronchogenic carcinoma, tumor metastases to the lungs, described as pulmonary osteoarthropathy or generalized osteophytosis, is a well recognized clinical entity. Theories of the factors responsible for the new bone formation have varied from that of toxic absorption from focal infections in the chest to changes in the acidbase equilibrium through decreased aeration as a result of compression of the pulmonary blood vessels, constriction of the bronchi, or of lung compression and collapse.

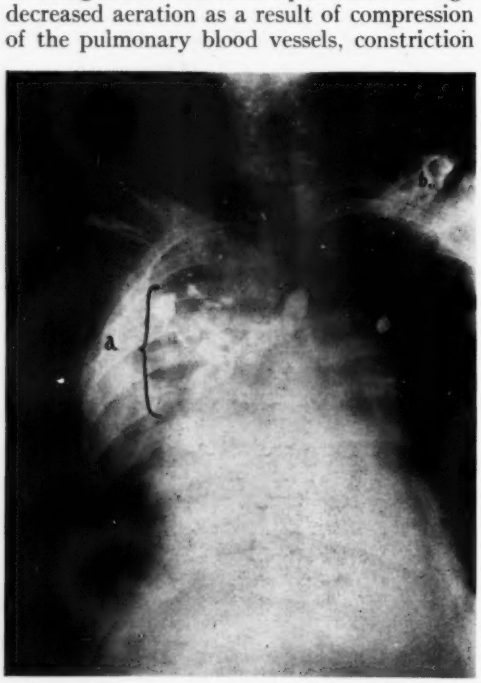

Fig. 1. Case 1. The sinus tract with an opening through the sternum has been injected. The opaque substance is seen to extend both upward and downward into cavities in the right side of the chest, *a*. The air containing tissue in this portion of the chest is obscured by either an effusion or a consolidation in the lung. Osteomyelitis of the left clavicle *b*, was also diagnosed from this roentgenogram.

Attempts to produce in experimental animals, the periosteal new bone, which is characteristic of this clinical syndrome, have been uniformly unsuccessful. A preliminary report of our study of the etiological factors in the production of these bone changes was published in 1931.

The following case reports demonstrate some of the different types of intrathoracic lesions which may be associated with the production of clubbed fingers and of this new periosteal bone. Detailed pathological studies were made of the bones obtained at autopsy in the 2 cases described.

CASE 1. De. S., male, aged 26 years, entered the University of Chicago Clinics May 2, 1928, complaining of skin eruptions on the neck, upper chest, and left arm, of 9 years' duration. Clubbing of the fingers was first noted about 5 weeks before coming to the clinic, and he complained of weakness, shortness of breath, loss of appetite, palpitation, and swelling of the ankles. Examination of the lesions over the chest revealed a sinus in the sternum from which pus could be expressed. There were a few râles in the chest posteriorly. Blood cytology and serology were normal. X-ray examination showed erosion and partial destruction of the left clavicle and beginning involvement of the left scapula. Blastomyces were found in the pus. Following treatment with sodium iodide, there was improvement in the skin lesions, but the sinus continued to drain profusely, and there was a daily rise in temperature to from 99.5 to 102 degrees. Pain in the abdomen and difficulty in breathing continued to be the outstanding symptoms and there was pitting edema over the lateral chest wall. On June 26, 1928, a diagnosis of massive empyema of the right chest was made. The white blood cell count at this time was 38,400. One thousand five hundred cubic centimeters of cloudy yellow fluid were removed from the chest and hemolytic streptococci were cultured from this. Roentgenograms of the chest following lipiodol injection of the sinus, October 12, 1928, showed extensive involvement of the right side of the thorax (Fig. 1).

Roentgenograms of July 31, 1928, showed periosteal new bone formation along the shaft of the

radius and ulna and of the tibia and fibula and this became more marked at each succeeding examination (Fig. 2). Chronic empyema persisted. The patient was discharged from the hospital October 31, 1928, and re-entered March 7, 1929. He had been confined to his bed during the interval of 5 months. The skin lesions had healed leaving dense scars, but the draining sinus in the sternum was still present. Blood chemistry studies were made at intervals from March 9, 1929, to March 21, 1929, the day before death occurred, and these showed blood calcium from 7.9 to 8.5 milligrams per cent, figures which are at least 20 per cent below normal for an adult, and inorganic phosphates of 3.69 to 4.42 milligrams per cent, slightly higher than the normal adult average (Table I). There was a slight increase in the carbon dioxide content from 66.9 per cent to 71.16 per cent and a corresponding shift of the hydrogen-ion concentration toward the acid phase from an initial reading of 7.62 (definitely more alkaline than normal) to 7.49. During the period of this blood study, the patient was dyspneic but there was no hyperpnea and the changes from normal indicate that there was inadequate aeration of the blood and hence accumulation of carbon dioxide in the tissues in spite of the fact that the patient was kept at rest. This lack of adequate oxygen intake and accumulation of acid products in the blood and tissues has been suggested as the etiological factor in the production of the bone changes. Renal function was not seriously impaired and the non-protein nitrogen, urea nitrogen, and blood chlorides were normal, rising only slightly on the day preceding death, March 21, 1929.

Autopsy. There was relatively little normal lung tissue containing air and the right lung was almost entirely destroyed by the long standing infection. The long bones were thickened. One tibia, fibula, and ulna were removed for study. X-rays of these bones revealed periosteal new bone formation entirely surrounding the shafts of the bones but absent at the ends of the shafts where there is known to be no periosteum. When these bones were cut longitudinally, the new bone was found to be from 1 to 5 millimeters in thickness and possessed a thin cortex with new cancellous bone filling in the space between

Fig. 2. Fig. 3.

Fig. 2, left. Case 1. There is marked periosteal new bone formation about radius and ulna and an appearance of increasing density or sclerosis in the shafts of these two bones. This periosteal new bone formation is noted also on all of the metacarpal bones and bones of the proximal phalanges. No bony changes are noted in the distal phalanges.

Fig. 3. Case 1. Photograph of the surfaces made by sectioning the tibia and fibula and ulna longitudinally shows a wide zone of periosteal new bone formation particularly on the medial side of the distal two-thirds and on the lateral side of the proximal two-thirds of the tibia and fibula and ulna with less new bone formation in the middle thirds and none at all adjacent to the articular surfaces.

Fig. 4. Case 1. Photomicrograph of a section of the distal end of the tibia. *A*, left, The outer portion of this new bone is slightly denser than that near the old cortex and a definite thin new cortex is forming. There is some smooth absorption of the old cortex on both the medullary and the outer surface with areas showing indentation and an occasional giant cell and lacunar absorption. There are very few cells of any kind and no infiltration of round cells. The type of the new bone which has formed is that which is usually seen at the site of an injury to bone. *B*, A higher power shows both absorption of the bone trabeculæ throughout the cancellous portion of the old shaft and definite new bone formation. The extra cortical new bone has been formed in irregular trabeculæ and the spongy bone is highly vascular particularly just outside the old cortex.

this and the old cortex which was still intact. The cortex and cancellous portion of the old shafts were grossly normal (Fig. 3). Microscopic sections of the tibia and fibula show the raised periosteum and the space between periosteum and the old cortex is filled with spongy cancellous bone which has surrounded the shaft, increasing its diameter by 30 to 50 per cent. There is slight absorption of the old cortex. The legends for Figures 4 and 5 describe the microscopic pathology.

This is the first case of which we have knowledge in which pulmonary osteophytosis has been demonstrated to be secondary to blastomycosis infection. In this case there was secondary infection from Streptococcus hemolyticus and the development of massive empyema with marked and prolonged respiratory embarrassment. The increase in carbon dioxide content and the gradual shift from a very alkaline hydrogen-ion concentration to one more nearly normal near the terminal stages of the disease adds some support to the theory that the bone changes which are characteristic of pulmonary osteophytosis may be due, in part at least, to a decrease in the oxygen available to the tissues and an increase in the carbon dioxide content. The presence of massive and prolonged chest infection is an argument in favor of the theory of toxic absorption as the primary etiological factor.

Case 2. J. B., aged 50, white male, entered the University of Chicago Clinics January 12, 1929, complaining of a lump on the right side of the neck of 1 year's duration and of additional swellings in the neck which had appeared more recently, associated with a yellowish discharge from the nose and similar discharge from a sinus at the site of the swelling in the neck. He had lost 50 pounds in weight and was weak and emaciated. He complained of dysphagia and dyspnea. Bloody material was expectorated from time to time.

Examination showed several distinct hard masses from 1 to 2 centimeters in diameter on the right side of the neck and a small mass in the left axilla. His fingers were clubbed and the skin was slightly cyanotic. The right side of the pharynx was distorted by the bulging of the mass and the right tonsil was pushed forward.

Blood serology was normal; white blood cells, 13,400; red blood cells, 3,500,000; and the urine contained hyaline casts and 2 plus albumin.

An X-ray of the chest showed a large pleural mass in the region of the left axilla with erosion of the ribs and an enlarged aorta (Fig. 6). Further X-ray pictures revealed a well marked pulmonary osteophytosis of the forearms (Fig. 7) and legs. These findings, together with the study of a section of

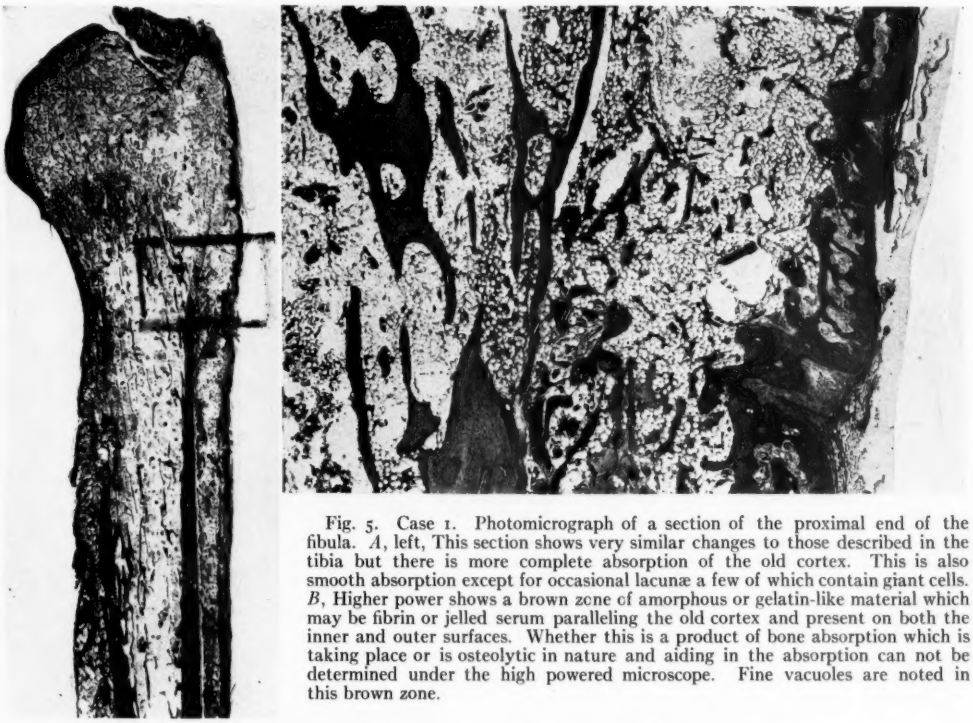

Fig. 5. Case 1. Photomicrograph of a section of the proximal end of the fibula. *A*, left, This section shows very similar changes to those described in the tibia but there is more complete absorption of the old cortex. This is also smooth absorption except for occasional lacunæ a few of which contain giant cells. *B*, Higher power shows a brown zone of amorphous or gelatin-like material which may be fibrin or jelled serum paralleling the old cortex and present on both the inner and outer surfaces. Whether this is a product of bone absorption which is taking place or is osteolytic in nature and aiding in the absorption can not be determined under the high powered microscope. Fine vacuoles are noted in this brown zone.

tissue removed at biopsy from the mass in the neck, led to a diagnosis of carcinoma with probable metastases to the mediastinum, ribs, axilla, and the brain stem and secondary pulmonary osteophytosis.

Blood chemistry studies were made (Table II). Changes from normal were similar to those noted in Case 1. Blood calcium was 6.75 and inorganic phosphates were 5.29. The carbon dioxide content was definitely increased to 67.0 and the hydrogen-ion concentration was alkaline, 7.61. The basal metabolic rate was +42, but, since the body temperature was 100 to 101 degrees, this was discounted. Respirations averaged 30 per minute and during the last 2 days these increased to 40 per minute. Bronchopneumonia developed and all day February 5, 1929, until his death at 4:00 p.m., there was marked dyspnea and cyanosis. A terminal decrease in the carbon dioxide content and the shift of the hydrogen-ion concentration toward normal may have been due to the increased respiratory rate, but the persisting cyanosis and dyspnea indicated that there was not a corresponding increase in oxygen that was reaching peripheral tissues.

Autopsy. Examination revealed a primary carcinoma of the nasopharynx with metastases to the neck, axilla, mediastinum, lungs, liver, brain, ribs,

TABLE I

Case 1. L. DeS. No. 4063, Age 27 years. Blastomycosis and pulmonary osteoarthropathy

Date	Ca	P	CO_2	pH	Remarks
3- 9-29	7.9	3.69	66.9	7.62	Blood 3 hours after lunch.
3-11-29	7.7	3.84	69.01	7.56	Before breakfast. N.P.N. 24; urea N 7; Cl_2 502.1
3-12-29	8.5	4.32	69.8	7.53	Before breakfast
3-13-29	8.5	4.42	71.16	7.49	Before breakfast. Intrav. No iodides given yesterday.
3-18-29					N.P.N. 29; urea N 13; chlorides 462.4.
3-21-29					N.P.N. 41; urea N 24.

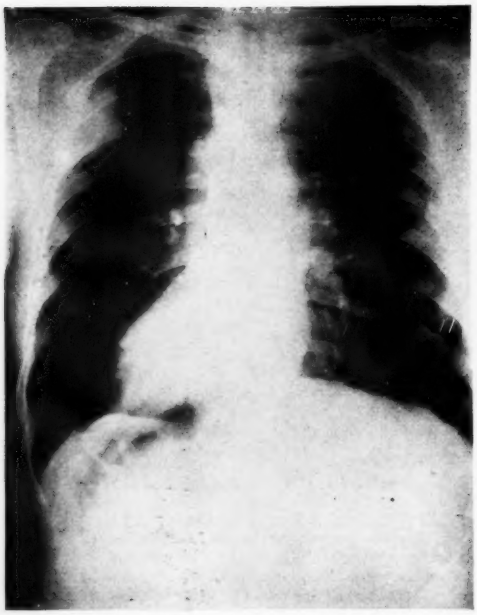

Fig. 6. Case 2. This X-ray picture of the chest of Case 2 was taken 3 weeks before death. There is a shadow at the hilum of the lung but the peripheral lung tissue does not seem to be involved. (This appearance of minimal involvement of the lung was confirmed at autopsy.) There is no obvious enlargement of the heart. This minimal cardio-respiratory pathology makes it more difficult for us to explain the dyspnea and osteoarthropathy which were present.

and the vertebræ. The bones of the forearm were removed and roentgenograms of the radii and ulnæ revealed extracortical or periosteal new bone formation (Fig. 8). When the bones were split longitudinally, the surfaces made by cutting the newly formed bone were similar to those described in Case 1. Microscopic sections were studied and these revealed new cancellous bone forming outside of the old cortex. The periosteum was raised and the spongy cancellous bone was similar to that found in the medullary portion of the old bone. A thin cortex was noted just beneath the raised periosteum. The cortex of the old bone was undergoing both smooth and, to a lesser extent, lacunar absorption. The changes were almost identical with those described in sections from the tibia and fibula of Case 1.

Although there was a small sinus at the site of the carcinomatous mass in the neck of this patient, the evidence of secondary infection was negligible. There was no empyema or other massive or chronic intrathoracic infection. Unless one assumes a possible toxic absorption from the carcinoma itself, we have here a case of extensive pulmonary osteophytosis without basis for the theory of toxic absorption to explain it. The factors common to both Cases 1 and 2 are respiratory embarrassment due to compression of a portion of one lung and some evidence of intrathoracic circulatory disturbance from mechanical pressure.

Fig. 7. Case 2. X-ray film of the hand showing periosteal new bone about the distal portion of the ulna and radius and also on the first metacarpal bone. The clubbing of the fingers can be seen but, as has been previously described, is confined to the soft parts and there are no definite changes noted in the bones of the distal phalanges themselves.

HISTORICAL REVIEW

Osteoarthropathy or osteophytosis is a non-suppurative affection of the extremities of the body found secondary to disease of the lungs, heart, or liver. Bamberger first described the bone changes characteristic of this disease in 1889 and Marie in 1890 named it hypertrophic pulmonary osteoarthropathy, although the most constant and striking changes produced are seen in the shafts of the long bones. Arnold suggested the name of secondary hyperplastic osteitis, but the condition has been referred to most often in the literature by the name of Bamberger-Marie's disease or the rather lengthy term devised by Marie.

In 1915, Locke collected 144 cases from the literature. Stephens, of the Mayo Clinic, collected 156 cases in 1928 and discussed the various theories which had been suggested to explain the etiology of the disease and attempted to reproduce the condition in dogs.

A study of these papers indicates the extensive changes which may occur in various tissues of the body secondary to chronic diseases of the lungs, heart, or, rarely, of the liver. The tissues affected include the skin and its appendages, the subcutaneous tissue, the joints, muscles, and the bones. *Clubbing of the fingers* is due to thickening of the soft tissue, for no bone change in the distal phalanx has been described, due possibly to the fact that this terminal digit has no periosteal covering. This change in the fingers is often associated with hypertrophy of the nails, the sweat glands, and pigmentation of the skin, and the nose may also be enlarged. *Joints* may be swollen and painful due to swelling of the synovia associated with a round cell infiltration and later erosion of articular surfaces. These changes may lead to limitation of motion and deformities, the most common being curvature of the spine. The latter deformity may be explained in most cases on a basis of the mechanical disturbance due to unilateral or bilateral disease of lung or pleura and is as often present without manifestations of osteoarthropathy as with it. *Muscle atrophy* and generalized weakness are probably secondary to the joint involvement and the debilitating effect of the disease and not to primary injury to the muscles themselves. *Bone changes* are striking and have been of most interest in the study of this disease. These consist of symmetrical proliferative periostitis, first involving the lower third of the diaphyses of the tibia, fibula, radius, ulna, the metacarpal and the metatarsal bones, and later the more proximal portions of the shafts

Fig. 8. Case 2. Bones of the forearm which were removed at autopsy and have been stripped of most of the soft tissue attachments. Periosteal new bone has formed particularly on the posterior surface of the ulna in its proximal and distal thirds. There is some evidence of beginning absorption of the outer portion of the cortex of the ulna and a thin but definite new cortical zone forming on the outer portion of the periosteal new bone. Less evidence of new bone formation is noted in the radius but it is more evenly distributed along the shaft of the bone and throughout its length. In the case of the ulna, there is some lamination or onion-peel appearance to the new bone that is formed, which is similar to that which is sometimes seen at the site of a Ewing type of undifferentiated round cell sarcoma.

TABLE II

Case 2. J. B. No. 9164 Age 50 years. Pulmonary osteoarthropathy

Date	Ca	P	CO_2	pH	Remarks
2 1-29	6.75	5.29	67.0	7.615	Blood before breakfast. Patient's respiratory distress not marked today
2 2-29	7.74	9.52	69.9	7.48	1½ hrs. after breakfast
2 4-29	8.59	6.33	67.9	7.36	Marked respiratory distress. Rapid respiration and gurgle in throat
2 5-29	Ins.	q—		7.355	9 a.m. Breathing stertorous
2 5-29	7.84	5.52	64.3	7.35	*Chlorides 543.2* 1½ hrs. before death. Resp. 60. Skin pale and clammy

Fig. 9. Dog 181. Shows complete collapse of the right lung persisting 7 months after the injection of 200 cubic centimeters of paraffin into the chest.

of the leg and arm bones. In advanced stages of the disease, the clavicle, the spines of the scapula and the vertebræ may be involved. Increase in length of the long bones has been reported.

MICROSCOPIC PATHOLOGY

The changes noted in the microscopic sections of the two cases which we have studied and described were well advanced. Stephens has described the early appearance of new bone formation in this disease. In its early state the new bone consists of thin layers which form immediately below the periosteum and, as the condition progresses, lie layer on layer around the bone. These layers tend to be heavier on the lateral than on the medial sides of the shafts, and heavier on the fibula than on the tibia, and are equally deposited on the radius and ulna. At first the layers of periosteal bone are distinctly separate from each other; they may accumulate until as many as six or more layers are present and distinguishable in the roentgenograms. In this stage the new bone is soft, very friable, and easily cut, or readily torn from the underlying cortex. It is very vascular and in performing a biopsy on a fibula a packing of gauze was necessary to control hemorrhage in one of the cases studied at the Mayo Clinic. In the advanced stage the new bone is firm but continues to present a picture of a second bone surrounding the old shaft with its zone of firm cancellous bone bounded by a thin, but hard, cortex under the raised periosteum. There are no longer distinct layers and the cancellous bone is irregular, but still very vascular. The old shaft retains its form, but is less dense, due to loss of lime salts and an increase in fat content. Shafts are increased in diameter and circumference.

ETIOLOGY

Pulmonary osteoarthropathy has occurred most commonly in young patients. Among the conditions which have been shown to be primary in the production of the peripheral changes which make up this syndrome may be listed: (1) tuberculosis of the lungs with cavities; (2) bronchiectasis; (3) empyema; (4) pneumonia; (5) pleurisy; (6) syphilis; (7) chronic valvular disease of the heart, especially when associated with passive venous congestion; (8) malignant tumors, such as carcinoma or sarcoma of the lungs; (9) and local circulatory conditions, such as aneurism, which may produce venous congestion. Other conditions described as primary, but which cannot be accepted as etiological factors without further evidence to support the contention include: (1) pyelonephrosis; (2) dysentery; (3) influenza (uncomplicated); (4) chronic jaundice; (5) alcoholism.

The following theories have been advanced to explain the changes noted in hypertrophic pulmonary osteoarthropathy:

1. Marie, Bamberger, and Symes-Thompson thought that a toxin was produced, probably by bacterial decomposition, and absorbed into the blood stream to produce the changes in the tissues characteristic of the disease.

2. Thayer considered it part of the picture of amyloid degeneration.

3. Massalongo believed that it occurred only in cases of arthritic diathesis and in this he was supported by Symes-Thompson.

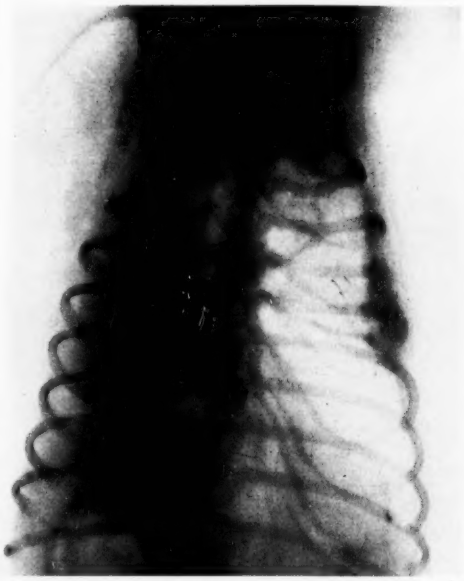

Fig. 10. Dog 795. Roentgenogram of chest 8 months after collapse of the left lung and subsequent removal of the lower and accessory lobes of the right lung.

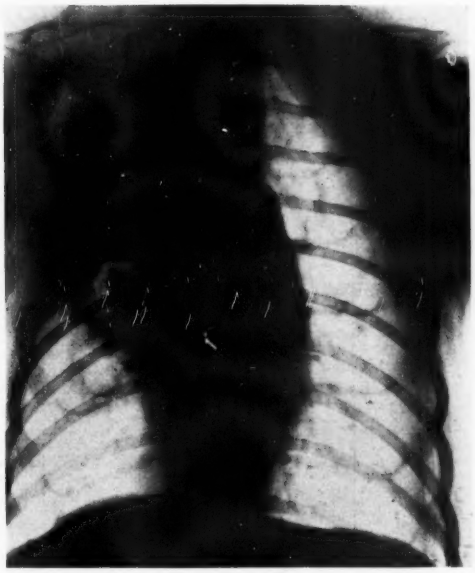

Fig. 11. Roentgenogram of dog's chest taken 3 weeks after direct inoculation of each of the right upper, middle, and lower lung lobes, through a thoracotomy opening, with 0.2 cubic centimeter of a heavy suspension of human tubercle bacilli (H119) in lipiodol. The right upper lobe bronchus was completely stenosed a few days before the picture was taken and the right upper lobe is completely atelectatic. The right middle and lower lobes each exhibit a large irregular thick walled abscess. The animal was sacrificed 5½ months later. At no time were there peripheral or X-ray evidences of generalized osteophytosis.

4. Thorburn called attention to the striking similarity between the periosteal new bone in osteoarthropathy and that which may be seen along the shafts of bones adjacent to tuberculous joints. He pointed out that postmortem examinations frequently confirmed the diagnosis of tuberculosis in patients showing these peripheral changes when tuberculosis had not been found in the course of clinical examinations, and, on a basis of these findings, he advanced the theory that all cases of osteoarthropathy were a form of tuberculosis which affected principally the long bones and the joints.

5. Berent suggested that the syndrome was due to a nerve disease and compared it to changes which are sometimes noted in syringomyelia.

6. Davis, Brooks, Kessel, Hyman and Herrick, Bryan, and Stephens have offered arguments and some evidence to support the theory that the changes in osteoarthropathy may be explained entirely on a mechanical factor of blood stasis. Campbell states, "Clubbing (of the fingers) is the result of defective oxidation in the tissues of the extremities, whether produced mechanically by obstruction to venous return, or as the result of a general lowering of the oxygen tension of the blood affecting parts of the body where normally the circulation is slow."

7. Bryan, Kleinberg, Marcus, and Phemister have expressed the opinion that at least two factors were necessary to produce hypertrophic pulmonary osteoarthropathy: First, a toxemia from a long standing disease in the chest and, second, circulatory disturbances resulting from either cardiac or pulmonary involvement.

8. Harter thought that the condition was due to lack of oxygen and called attention to the somewhat similar changes found in some people living in high altitudes where oxygen is rare.

TABLE III.—RESULTS OF INJECTING PARAFFIN INTO PLEURAL CAVITY

This table shows blood chemistry studies of the three dogs surviving for the longest period. There were no consistent changes in the acid base balances or the calcium and inorganic phosphate content of the serum.

Dog No.	Date	Days transpired	Blood serum chemistry					Comment
			CO_2†	pH	Ca*	P*	Ca x P	
181	11–29–29		59.0	7.5	12.2	5.1	61.7	Normal—fasting
	1–3–30			7.5	11.7	5.1	59.8	Normal—fasting
	3–13–30		50.6	7.5				200 c.cm. paraffin injected into right pleural cavity
	3–27–30	14	50.1	7.5	12.1	5.1	61.1	Normal. No dyspnea
	12–2–30	253	51.1	7.4	11.5	6.2	71.3	No arthropathy
	1–22–31	301	50.9	7.4	12.2	5.2	63.0	2–25–31 Right chest flat to percussion. X-ray shows no air in right chest, but no evidence of periosteal new bone
	5–6–31	405	43.7	7.4	10.9	5.4	58.4	No arthropathy
520	11–29–29		52.9	7.5	11.9	4.8	57.1	Normal
	1–3–30			7.6	11.8	5.6	66.1	Normal
	3–13–30		50.7	7.6				200 c.cm. paraffin injected into right pleural cavity
	3–28–30	15	53.2	7.5	12.2	4.8	53.1	Excellent condition
	4–10–30	27	42.7		11.5	5.9	67.5	Hemolysis of blood
	7–14–30	121			10.9	5.0	54.5	No arthropathy
	12–2–30	138	49.6	7.4	12.1	4.9	59.0	
	1–22–31	180	45.4	7.4	12.5	4.4	55.5	2–25–31 No arthropathy. Very little air in chest
	5–6–31	284	42.2	7.2	11.7	5.0	56.2	
33	8–12–30				10.8	5.0	54.0	250 c.cm. paraffin, right chest
	12–2–30	110	51.9	7.5	12.3	6.1	74.5	10–6–30 No changes at lower end of tibia or fibula
	1–22–31	160	50.7	7.3	12.3	6.5	79.3	2–25–31 X-ray shows no bone changes. Chest looks clearer
	5–6–31	264	50.1	7.5	12.5	5.6	64.8	

*Milligrams for each 100 c.cm. †Volume per cent carbon dioxide content.

EXPERIMENTAL STUDIES

Attempts to produce in experimental animals changes characteristic of the clinical syndrome of hypertrophic osteoarthropathy have been uniformly unsuccessful.

Bamberger, believing a toxin to be the cause of the bone changes, injected into the rectum of 3 young rabbits twice daily a bronchiectatic secretion secured from 1 of his patients, but did not produce any of the changes.

Phemister injected cultures of various organisms including Streptococcus viridans and Streptococcus hemolyticus into rabbits for a period of 6 weeks without producing any bone changes.

Stephens tried to support his theory that all of the changes noted could be explained on a basis of peripheral blood stasis. He produced mechanical interference with the venous flow of blood in dogs creating venous congestion in the extremities, but was not successful in producing a proliferative periostitis.

Harter and Churchill sought to produce the changes by ligating and sectioning the bronchus in cats and monkeys and in other ways tried to create a lowered oxygen content in the peripheral blood, but they were not successful in producing any changes in the bones, nails or capillaries of the nail beds.

We attempted to produce the syndrome of hypertrophic pulmonary osteoarthropathy in dogs by creating intrathoracic complications which are similar to those which in the human being have been found to predispose to the development of clubbed fingers and periosteal new bone formation.

Roentgenograms were made of the bones of the extremities both before and at intervals after the operations on the chest, and the calcium and inorganic phosphate and carbon

TABLE IV.—RESULTS OF COLLAPSE OF LUNG BY STENOSIS OF BRONCHUS

Dog No.	Date	Days transpired	Blood serum chemistry					Comment
			CO_2†	pH	Ca*	P*	Ca x P	
847	7–14–30				10.5	4.5	46.5	7–15–30 Stenosis begun 8–28–30 Complete stenosis
	9–19–30	64		7.6	10.1	5.0	50.0	11–5–30 No arthropathy
	11–10–30	115	46.4	7.5	11.3	2.8	31.3	
	2–18–31	213	46.0	7.2	10.2	2.9	30.0	2–24–30 Negative X-rays
	5–13–31	308	48.7	7.4	11.0	4.2	46.3	No new bone formation
400	3–27–30			7.6	12.1			35% $AgNO_3$ to stenosis accessory and right mid-bronchi
	4–10–30	13	38 4		10.9	4.9	53.9	Sl. hemolysis. Rt. lower bronchus cauterized. 6–19–30 stenosis complete, right
	7–2–30	105	42.4		10.2	5.5	56.3	
	9–19–30	182		7.5	10.6	4.5	48.0	
	11–10–30	233	38.8	7.5	11.0	4.0	44.2	11–3–30 X-rays show no periosteal change
	2–18–31	331	33.3	7.2	10.8	2.8	30.7	2–24–31 No definite bone change
	3–2–31	345	38.9	7.2	10.8	4.0	42.8	No periosteal new bone
870	7–14–31				10.5	4.8	50.0	Stenosis (right prim.) begun 7–15–30
	9–19–30	65		7.5	10.8	5.3	56.9	9–17–30 Total collapse and complete stenosis. 11–5–30 X-rays show no arthropathy
	11–10–30	116	47.5	7.5	11.4	5.4	61.6	
	2–18–31	184	46.1	7.2	10.5	5.0	52.2	2–24–31 X-rays negative
	5–13–31	269	48.1	7.4	10.8	4.4	47.7	No osteoarthropathy
795	2–24–31							X-rays—very little air in lung. No osteoarthropathy
	3–2–31	8	45.6	7.2	10.5	5.5	58.0	Collapsed left lung—right lower and accessory removed
	5–13–31	79	53.8	7.5	11.7	5.8	67.4	No osteoarthropathy

*Milligrams for each 100 c.cm. †Volume per cent carbon dioxide content.

dioxide content and the hydrogen-ion concentration of the blood serum were determined.

Of 9 dogs into whose right pleural cavity from 100 to 300 cubic centimeters of paraffin was injected, 1 survived 9 months and 2 were sacrificed after 18 months. In each instance, in addition to the mechanical pressure on the lung by the paraffin, there was a prompt pleural effusion which almost completely compressed the lung in the right half of the chest, and displaced the heart and the mediastinum to the left, reducing the air space in the left side of the chest (Fig. 9). No consistent or significant blood changes were noted following the injection of the paraffin (Table III). No periosteal new bone formation or other changes characteristic of osteoarthropathy were observed.

By means of a method described by one of us, collapse of one or more lobes of the lungs of 13 dogs was accomplished. One of the dogs developed a lung abscess, and lobectomy was performed upon 5 dogs at varying intervals following collapse of the lobe or of the corresponding lung. Roentgenograms of the chest of each dog showed the diminished air containing lung tissue. Figure 10 is the X-ray of the chest of a dog following collapse of the left lung after stenosis of the bronchus by means of silver nitrate cauterization and subsequent removal of the right lower and accessory lobes. Only the right upper and middle lobes of the lung contain air, and yet this dog was not dyspneic and no osteoarthropathy developed. The animals in this series were exercised vigorously each day for several weeks by being forced to swim in a tank, but in spite of this forced exertion which did produce temporary dyspnea there were no significant changes in the blood chemistry determinations. The results of four of these studies are included in Table IV. As will be noted from this table, for a few days to a few weeks after the functioning lung tissue had

been reduced to a minimum, there was a definite change in the hydrogen-ion to the acid side of normal. These dogs seemed to be able to adjust themselves to the change very quickly for the hydrogen-ion concentration returned to normal and temporary signs of respiratory embarrassment disappeared.

Twenty-eight dogs were successfully inoculated with tubercle bacilli and abscesses produced in the lung in each instance (Fig. 11), and empyema in the chest in one dog, but in no instance were we successful in producing any of the peripheral or bone changes which are characteristic of the clinical syndrome of hypertrophic pulmonary osteoarthropathy.

EVALUATION OF STUDY

The clinical syndrome known as secondary hypertrophic pulmonary osteoarthropathy usually develops in association with chronic intrathoracic disease. The most common primary diseases leading to the changes characterized by clubbing of the fingers and periosteal new bone formation along the shafts of the radius and ulna, fibula, and tibia and less often the metacarpal or metatarsal bones are: bronchiectasis, empyema, and tuberculosis with cavities in the lungs. There is usually definite evidence of both circulatory and respiratory embarrassment including dyspnea, venous congestion and cyanosis in the distal portion of the extremities. The concomitant occurrence of infection and usually of suppuration in the thorax has led to the theory that absorbed toxins were at least in part responsible for the more peripheral changes in the bones and soft tissues. Reports of cases with well advanced hypertrophic osteoarthropathy secondary to malignant growths such as sarcoma or carcinoma of the lung without abscess formation or other chronic infections discredits the toxin theory. The only constant finding is that of disturbed circulation and, in most cases, dyspnea as well as cyanosis. We not only failed to produce the osteoarthropathy in experimental animals but were unable to bring about prolonged dyspnea or cyanosis or changes in the acid base equilibrium. In the cases which we have studied there was an increase in the carbon dioxide content of the serum and, except toward the terminal stages of the disease, a change in the hydrogen-ion concentration toward the alkaline side. After a review of other theories and of the findings in the cases which we have studied, we are inclined to support the theory that these changes noted in our cases were due to decrease in the oxygen content of the serum and may have been due to a corresponding increase in waste products of a metabolic nature. The report of clubbing of the fingers and of periosteal new bone formation in individuals who have no known intrathoracic complications, but who live at high altitudes where the air is rarefied, supports this hypothesis.

We have tried without success to produce hypertrophic pulmonary osteoarthropathy: (1) by pressure upon a lung from a foreign body in the pleural cavity; (2) stenosis of a primary or secondary bronchus; (3) collapse or total absence of a lobe or of an entire lung; (4) pleurisy with effusion; (5) empyema and solitary lung abscess. In the human subject any of the above intrathoracic complications might be expected to produce respiratory embarrassment with varying degrees of dyspnea, cyanosis, and venous engorgement in the tissues most distant from the heart. None of these changes were noted in the experimental animals which seemed to be able to compensate for loss of functioning lung to a surprising degree, even when forced to vigorous exercises, such as continuous swimming for an hour or longer.

Godlee has reported complete recovery of an advanced case of hypertrophic pulmonary osteoarthropathy after healing of an empyema cavity following removal of a piece of rubber drain that had been retained there for several years.

SUMMARY

1. Hypertrophic pulmonary osteoarthropathy is usually secondary to intrathoracic disease.

2. Such diseases are usually of long standing before the changes in the extremities are noted.

3. Infection or suppuration is not essential to the production of osteoarthropathy.

4. Two cases are reported: one of blastomycosis of the chest wall with secondary infection and empyema; and a second of

carcinoma of the lung with involvement of the bronchi and larger blood vessels but no intrathoracic suppuration. The conditions common to both cases were dyspnea and cyanosis and a disturbance of the acid base equilibrium of the peripheral blood.

5. Intrathoracic complications were created in dogs but we were unable to produce dyspnea or cyanosis, and blood chemistry studies showed no consistent or sustained variation from normal. Although chronic abscess and empyema were produced in the chest of some of the dogs, there was no suggestion of clubbing of the phalanges, edema or periosteal new bone formation in any of these animals and the animals quickly recovered from dyspnea which was brought on by strenuous exercise.

6. The bones of the extremities of 2 clinical cases of hypertrophic pulmonary osteophytosis which were examined at autopsy were studied both grossly, by X-ray and microscopically. These showed a chronic proliferative osteitis with a shell of new cancellous bone 1 mm. to 5 mm. thick completely surrounding the tibia, fibula, radius and ulna. A thin new cortex was present just beneath the raised periosteum.

7. No conclusions can be drawn from this series of cases or from the negative results obtained in our experimental studies, but we are led to add our opinion that the secondary changes of osteoarthropathy are not due to a toxin, but can be explained on the mechanical basis of blood stasis or of poor aeration of the blood creating changes in the acid base equilibrium.

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PREGNANCY COMPLICATING DIABETES

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PREVENTION of the death and decay of the over-ripe fetus of the diabetic mother is a challenge today to the obstetrician and research worker in the field of diabetes. Maternal mortality attributable to the disease has been conquered in the insulin era, but stillbirths and the macerated fetus of the giant type are nearly as characteristic of diabetic pregnancies which are allowed to come to full term today as they were in the pre-insulin era.

Two hundred fifty-seven pregnancies have occurred in 180 diabetic women in the series of patients seen by Dr. Joslin, from 1898 to October 10, 1934. One-half of these occurred in the pre-insulin and one-half in the insulin eras. Of this number, 66 were under our immediate care. The series differs from others which have been published because it includes 22 pregnancies in 15 patients who had onset of the disease in childhood. The age at onset of the diabetes in this special group varied from 8 to 14 years, and the duration of diabetes at onset of pregnancy from 2 to 14 years. This small group is unique and we believe forewarns us of the problems of the pregnant diabetic woman of the future.

TABLE I.—OUTCOME OF PREGNANCIES DELIVERED AT TERM

(1) Non-diabetics, (2) our patients prior to onset of diabetes, (3) in diabetics in the pre-insulin, (4) in the insulin eras, and (5) in diabetic patients directly under our care.

	Living births per cent	Stillbirths per cent
1. Johns Hopkins series of *2885 consecutive cases (used as a control group)	94	6
2. Our patients prior to onset of diabetes	80	20**
3. Pre-insulin era	71	29
4. Insulin era	79	21
5. Patients under our immediate care	89	11

*Peckham, C. H. Bull. Johns Hopkins Hosp., 1934, 54: 186.
**Undoubtedly includes early undiagnosed diabetes.

Scope of problem. The problem of pregnancy complicating diabetes is increasing in importance. There are some 100,000 (14) diabetic women of childbearing age in the United States, and if the known pregnancy rate of our own series, which is 10 per cent, may be applied to the diabetic population at large, the problem directly concerns some 10,000 diabetic women, or 1,500 annually. That diabetes does play a menacing rôle in the successful outcome of pregnancy is unquestionable. In our own series of patients, this is evident in a comparative analysis of diabetic pregnancies and pregnancies in a non-diabetic series, and also in a comparison of pregnancies in our own patients prior to, and following, the onset of the disease.

Although Table II shows only a slight improvement of the insulin era over the pre-insulin era in all cases, this does not indicate a failure of insulin therapy but rather its success, for the inclusion of a large series of severe diabetics of the new generation of youthful diabetics, and the long duration cases, alter comparative statistics. Some of these pregnancies could not have occurred and others would have been interrupted in the pre-insulin era.

TABLE II.—COMPARISON OF PREGNANCIES IN OUR PATIENTS

(1) Prior to onset, (2) after onset in the pre-insulin and (3) in the insulin eras, and (4) under our own care.

	Living births		Stillbirths		Miscarriage or abortion	
	No.	Per cent	No.	Per cent	No.	Per cent
1. Prior to onset of diabetes	115	72	27	17*	18	11
2. Pre-insulin era**	57	56	23	22	23	22
3. Insulin era†	69	66	18	17	18	17
4. Our cases‡	44	77	5	9	8	14

*See note "Stillbirths," Table I.
** Died undelivered, 7 patients; end-result unknown, 15; therapeutic abortions, 5.
† Unknown, 9; therapeutic abortions, 13.
‡ Therapeutic abortions, 7.

Physiology of pregnancy. Many physiological processes of pregnancy are capable of aggravating a pre-existing fault of sugar metabolism. Pregnancy, which is a great strain upon the metabolism of carbohydrates for the non-diabetic women, of necessity is a far greater carbohydrate strain for the diabetic. Notable in this respect is the rise of the basal metabolic rate due either to the growth of the products of conception (38), although this does not explain the rise which continues after delivery, or to the hyperactivity of the thyroid, pituitary, and adrenal glands. Microscopic changes, indicative of increased activity of the thyroid gland during pregnancy, and biological assay measuring an increase of the secretion of this gland have been demonstrated. When carbohydrate metabolism is at stake protein and fat metabolism will also fail. Even in the non-diabetic, the alkali reserve drops and ketone bodies (38) appear in the blood and urine. With such a background, it is remarkable that the successful termination of pregnancy has occurred in as many as two-thirds of all our diabetic cases.

Many questions of practical, theoretical, and ethical importance arise in this study and at present the answers are often speculative rather than determined. First, what is the relative fertility of the diabetic? Second, when does the glycosuria of pregnancy indicate true diabetes? Third, is pregnancy a precipitating cause of the disease? Fourth, what is the effect of diabetes upon the outcome of pregnancy? Fifth, what is the effect of pregnancy upon the course of diabetes and upon the future health of the diabetic woman? Sixth, what is the best method of diabetic and obstetric management? Seventh, what is the effect of the disease diabetes upon the future health of the child? Eighth, what are the child's chances of inheriting diabetes?

Fertility in diabetes. The lack of fertility of the diabetic woman, which was long recognized in the pre-insulin era, has in great measure been corrected in proportion to the extent of the control of the disease. In uncontrolled diabetes, delayed maturity and long periods of amenorrhea still occur, but unlike what occurs in other diseases, the normal menstrual cycle of the diabetic can be re-established even after a cessation for a period of years. The total pregnancy rate in our series is 10 per cent and the yearly rate 1.5 per cent.

Although in our own series the pregnancy rates in the insulin and pre-insulin eras are essentially the same, the clinical picture is different because the severe diabetic did not become pregnant prior to insulin therapy. The pregnancy rate in the pre-insulin era in the series of other authors has varied from 2 per cent in the London Hospital (35), and 5 per cent in Von Noorden's cases (20), to 6 per cent in Lecorche's (17) series of patients. The increase in the insulin era was greater in the London Hospital series than in ours, the former having risen to 15 per cent and the latter to 10 per cent, whereas the Mayo Clinic (23) in 1926 reported only 4 per cent.

The underlying cause of lack of fertility in uncontrolled diabetes is not definitely known. The basis may be hormonal, dietary, or nutritional. Either excess or lack of pituitary prolan is a possible cause. Depression of the activity of the other endocrine glands probably occurs when diabetes is uncontrolled and the patient undernourished. The appearance of the diabetic dwarf is thus presumptive evidence of a functional hypoactivity of the pituitary gland. Hypoactivity of the gonadotropic factor of the pituitary would result in lack of estrin. Parisot has described the disappearance of graafian follicles in diabetes. Atrophy of the uterus has been described by von Grafe, and we have observed lack of development of the genital tract at autopsy in 4 young patients whose diabetes was of long standing. Under insulin therapy and adequately controlled diabetes, not only has long standing amenorrhea disappeared, but pregnancies have occurred in such cases, and, even more remarkable, in 2 of our pseudo dwarfs (Case 8256 and Case 6319).

Diagnosis of glycosuria. The recognition of diabetes during pregnancy may be difficult indeed, for starvation, hyperactivity of the thyroid, pituitary and adrenal, and depletion of glycogen occur, and each one is capable of lowering tolerance for sugar. Glycosuria, apparently benign in nature, occurs so commonly in pregnancy that some writers go so far as to

say that if enough specimens of the urine of the pregnant patient are examined, one or more will be found to contain sugar in amounts varying from traces to several per cent, and yet the blood sugar remains normal. The reported incidence of glycosuria in non-diabetic pregnancies varies from 35 per cent (25) to 66 per cent (7) and in these statistics the sugar was identified as glucose.

Hyperglycemic curves after sugar tolerance tests have been reported by Pillman-Williams and Richardson, who classify them as benign. Skipper has demonstrated a plateau curve. In our own series of patients, the diagnosis of diabetes is made as in all other patients on the rise or peak of the curve. Whether the curves are normal or abnormal, the patient should be observed for a period of years.

Pregnancy as a cause of diabetes. Since only 5 per cent of our female patients of childbearing age have had onset of diabetes during pregnancy, pregnancy does not appear to be an inciting or at least a common inciting cause of diabetes. Potential diabetics (27, 40) (the children of two diabetics, the homologous twin of a diabetic) have not developed the disease at this time and, under 45 years of age, more males than females contract diabetes (Table III). The reverse would be expected if pregnancy precipitated diabetes.

TABLE III.—SEX AND THE ONSET OF DIABETES

Decade of onset of diabetes	Male per cent	Female per cent
1	5.0	4.4
2	7.5	6.1
3	9.3	6.5
4	14.7	11.2
5	23.1	24.1

Diabetes incidence increases, however, at other times when the pituitary prolan of the blood is high and at such times an existing diabetes is often made more severe, for not only is the peak of incidence in females at 12 (39) and 50 (14), but diabetes is increasingly difficult to control during catamenia and at the time of menopause.

Effect of diabetes upon the course of pregnancy. The background of diabetes favors the development of the accidents of pregnancy in proportion to lack of control of the disease. Abortions and early miscarriages occur with relatively greater frequency in diabetic women after onset of the disease. Twenty-two per cent of our patients aborted in the pre-insulin era, compared with 17 per cent in the insulin era, and 11 per cent in these same women prior to the onset of diabetes.

Premature expulsion of the fertilized ovum may be due to diabetic or non-diabetic causes. Among the diabetic causes we must consider a lethal factor in the egg, hypoglycemia, acidosis, deficiency diet, or lack of glycogen. The non-diabetic factor which, however, might secondarily be due to diabetes is excess of pituitary prolan A with consequent depression of the function of progestin. If the fault lay in the primary cell because of diabetes, one would expect the wives of diabetic men to abort as frequently as do diabetic women, and this is not the case. Lack of glycogen is possible. The studies of Simon show that the fertilized ovum implants itself in that portion of the uterus which has the richest supply of glycogen. In uncontrolled diabetes, glycogen deposition is abnormal. Faulty nidation may result from depression of progestin.

Hypoglycemia (30), though capable of starting uterine contractions, probably is not an important factor, because abortions occurred even more frequently in the pre-insulin era. It appeared to be the cause of abortion in one patient, Case 7242. Two other patients, Case 8256 and Case 3040, had hypoglycemia with loss of consciousness and convulsions, and were delivered of living babies at term.

Acidosis appears to be somewhat more harmful. However, only 5 of the 15 patients who miscarried had acidosis, including one with chemical coma. Twelve had poorly controlled diabetes. The true accidents of diabetes thus appeared to play a minor rôle in the termination of early pregnancies. Factors secondary to uncontrolled diabetes, such as faulty storage of glycogen and disturbed endocrine function, need further investigation, and in fact, this study has already been started.

Stillbirths. The investigation of the cause and the means to prevent the occurrence of stillbirths in diabetics is the most important problem in pregnancy complicating diabetes.

The incidence of stillbirths has not been reduced adequately in the insulin era since 17 per cent of the pregnancies resulted in stillbirths when even 6 per cent is considered a high stillbirth rate. In patients under our care, it has been reduced to one-third of the rate of the pre-insulin era and insulin era as a whole, but it still occurs twice as frequently in diabetics as it does in non-diabetics (see Tables I and II).

Mechanical, chemical, hormonal, or structural abnormalities may cause stillbirths in diabetes. Maternal complications such as syphilis, heart disease, and anemias were not found in this series. Of the mechanical factors, the size of the baby is the most important. Sixty per cent, or 33, of our babies, for whom we had data, weighed over 8 pounds, compared with 9 per cent of 100 babies reported by Carreno for a series which included one diabetic. The average weight for babies in the insulin era slightly exceeded the weight of babies in the pre-insulin era. The size of babies (2) of diabetic mothers is so striking that some clinicians call attention to the fact that a large baby may indicate maternal diabetes, and such mothers should be investigated for the disease. Nevinny and Schretter have reported a baby classified as a giant, and observed changes in the fetal hypophysis. Obesity of the fetus in the diabetic may be due to overnutrition from hyperglycemia, lipemia, or to edema which is a direct result of exogenous insulin. Possibly it is inherited obesity. Perhaps it is due to hyperactivity of the fetal or maternal pituitary gland. Permeability of the placenta to fat and pituitary-like substance is known. Exogenous insulin is not the likely cause because the babies in the pre-insulin era were large. The greatest growth of the embryo occurs in the last 2 months, at which time the blood sugar is generally normal. Extreme hyperlipemia has not been observed in our own pregnancy cases. Thus insulin, fat, and sugar do not seem to be the probable causes of the overgrown fetus. The mechanical difficulty of labor resulting from the delivery of the large baby, cannot be the most common cause of fetal death, though undoubtedly it increases the stillbirth rate. Two-thirds of these fetuses were macerated, or an incidence of 1 in 7 in the insulin era compared with an incidence of 1 in 83 for non-diabetics, reported by Dippel from the obstetrical service of the Johns Hopkins Hospital. This leads us to search for a cause which might interfere with the nutrition of the child or a direct lethal agent, active the last 4 weeks of pregnancy. Small placentas which might result in subnormal nutrition have not been found in our cases.

Hydramnios, which also endangers the life of the fetus, is believed to occur in diabetes, and is held as a cause of fetal mortality. We have observed it but twice. This is surprising because the common causes of hydramnios, namely fetal deformities, large children, and maternal toxemias occur in diabetes. The origin may be chemical. Grafe has demonstrated an excess of glucose in the amniotic fluid in 5 of 10 diabetic pregnancies. Better control of glycemia may have resulted in correction of this complication.

The abnormal chemistry of the maternal blood may have its effects upon the fetus. Reports exist to the effect that maternal and fetal blood sugar and alkali reserve are the same and that the low alkali reserve is the factor which kills the fetus in toxemias of pregnancy. The blood of the newborn baby and maternal bloods in 3 of our cases show the following:

In this small series the level of the blood sugar, plasma carbon dioxide combining power, non-protein nitrogen, cholesterol and chloride of the baby and mother were not identical. Thus we have no proof that imbalance of carbohydrate, fat, mineral metabolism, or acidosis of the mother directly influences the child (Table IV).

In the insulin era Cases 12751, 7565, 3677, 2776 developed coma during pregnancy. In the 3 former, coma was not followed by death of the fetus. Stillbirth was the outcome of Case 2776, but the fetus was macerated and death of the fetus antedated the onset of coma.

Although the passage of insulin through the placenta has been demonstrated, the production of hypoglycemia in the fetus does not seem probable. Britton injected large amounts of insulin, producing maternal hypoglycemia

TABLE IV.—A COMPARISON OF CHEMICAL DATA IN MOTHER AND INFANT

Case 7251 Sept. 4, 1934	Blood sugar per cent	Vol. per cent Plasma CO_2 combining power	Non-protein nitrogen mgm. per 100 c.cm.	Chloride mgm. per 100 c.cm.	Cholesterol mgm. per 100 c.cm.
Infant (Cord)	0.14	19			
Mother	0.20	36	29		
Placenta	0.16	28	38		
Case 11033 Sept. 10, 1934					
Infant (Cord)	0.10	32	32	584	
Mother	0.13	23	27	556	
Placenta	0.08	29	29	607	
Case 11563 Sept. 14, 1934					
Infant (Cord)	0.07	38	24		50
Mother	0.10	30	33		260

with little or no apparent effect upon the fetus. Certainly none of our own patients had severe hypoglycemia as an attributable cause of stillbirth. Furthermore, Plais and Woods have shown that in a pregnant woman near term, starvation for 50 hours in the last month of pregnancy is frequently followed by hypoglycemia and onset of labor, without injury to the fetus. The report of Gray and Feemster and others suggesting that endogenous hypoglycemia is a cause of fetal death is an interesting possibility. Better control of diabetes has certainly reduced the stillbirth rate. Pathological evidence in favor of this theory is striking but the normal fetal pancreas has large islands, and the newborn and premature infant relatively low blood sugar levels.

Disease of the uterus, age of the mother, parity, or duration of diabetes, may be factors producing any of the failures. Age of the mother had its effect, since the younger and older mothers lost more children than did the intermediate group.

Multiparity had no favorable effect. The outcome of multiparous pregnancies showed only 50 per cent successes. The outcome of primiparous pregnancies without cesarean section was 69 per cent, and with cesarean section was 75 per cent.

Factors which favor ready control of diabetes, favor the number of live births. This is

TABLE V.—AGE OF DIABETIC MOTHERS IN RELATION TO SUCCESSFUL OUTCOME OF PREGNANCY

Age in years	Successful outcome of pregnancy per cent
Under 20	35
20–30	35
30–40	60
40	50

apparent in both the pre-insulin and insulin eras. In the first year of diabetes, the disease is most readily controlled, and here we find the greatest number of live births. In the insulin era the same is true. The percentage of live births is 85 in the first year of the disease, and drops to 50 per cent in all other years of diabetes.

The demonstration of excessive prolan in the blood and urine of patients with toxemia by Smith and Smith, and the excess of toxemias and eclampsias in diabetes in our own series of cases, give us a new lead in the search for the lethal factor active the last 4 weeks of diabetic pregnancies. In accordance with this theory of possible damage to the fetus from excess of prolan is the result of the experiment of Snyder who found that the administration of prolan (antuitrin S) to pregnant rabbits resulted in prolongation of gestation and of death and maceration of giant postmature rabbit fetuses.

Maternal mortality in contrast to the high fetal mortality has been low. In the combined eras it was 5 per cent, in the pre-insulin era 5 per cent, and in the insulin era 5 per cent. The deaths in the pre-insulin era were all diabetic; the deaths in the insulin era were all obstetric.

Maternal accidents. The background of diabetes appears favorable to the development of toxemia and eclampsia, the incidence of eclampsia being 5 per cent compared with an average of 0.3 per cent in a non-diabetic series. The younger the patient the greater the chance for development of eclampsia because the incidence in former juvenile diabetics was 13 per cent. It is possible that diabetics are predisposed to develop an endocrine imbalance similar to that described by Smith as typical of toxemia and eclampsia.

Pernicious vomiting has occurred but once. Premature separation of placenta and extrauterine pregnancies have not occurred. There was but 1 breast abscess, and 3 cases of puerperal sepsis.

The effect of pregnancy upon diabetes. (*a*) *Tolerance.* This brings us to the next problem, the course and treatment of diabetes during pregnancy. The question whether or not pregnancy alters the course of diabetes is still debated. In the literature (8) one finds reports of gains in tolerance for carbohydrate and an equal number of reports of losses of tolerance for carbohydrate. The fairly general concensus of opinion is that a loss occurs in the first trimester, a status which is stationary in the second, and either a gain or loss of tolerance in the third. In the pregnant diabetic dog, Carlson and Drennan were able to demonstrate a great gain in tolerance during pregnancy. That insulin circulates through the placenta of the mother is shown in the experiment of Pack and Barber. Insulin injected into the fetus of a goat was followed by the production of hypoglycemia in the mother. Some few patients in our series, notably one after coma, Case 7565, omitted insulin entirely in the last trimester. A crude analysis of our cases shows that half of the number with suitable records had milder diabetes during pregnancy than at any time before or after, but others have had more severe diabetes. Furthermore, we observed one patient, Case 6506 for some weeks after the death of the fetus, and her insulin requirement did not alter.

During the course of pregnancy in the severe juvenile type of diabetes, there has practically never been a gain of tolerance for carbohydrate. The weight of the newborn baby's pancreas is only 1.5 grams; the weight of the adult pancreas is 100 grams. If we assume that 100 units of insulin are produced by the 100 gram pancreas of an adult, 1 unit is produced per gram. The child's pancreas, on this basis, would hardly secrete more than a single unit. Fetal pancreas, however, probably contains 10 to 15 times as much insulin as adult pancreas. In all cases this constant source of insulin would be of value. It would be an adjunct to treatment in twin pregnancies, as in the case reported by Lawrence (15, 16). Our own patient with twin pregnancy showed no great gain in tolerance. The multiple pregnancies of animals may account for the gain reported by Carlson and Drennan. Under-nutrition may explain whatever gain in tolerance occurs (1, 18). We thus conclude that a gain or loss of tolerance is an individual factor.

Effect of pregnancy upon the direct complications of diabetes. (*b*) *Acidosis.* The direct complications of diabetes, coma and hypoglycemia, are to be feared during pregnancy, labor, and the puerperium. Acidosis and coma are to be feared during pregnancy because a low alkali reserve, glycogen depletion, and increased metabolic rate occur.

The plasma combining power for carbon dioxide was found to be low in 12 of 13 patients carefully studied, and 6 had clinical signs of coma. These patients demonstrated that the blood sugar was not proportionately high. If coma occurs during the course of labor, treatment is difficult, for labor deepens coma. As soon as delivery is completed chemical recovery follows.

(*c*) *Hypoglycemia.* Hypoglycemia in pregnancy is usually the result of poor treatment. It occurs when the dosage of insulin is increased in the presence of a low renal threshold. During labor it results from increased utilization of carbohydrate, and during the puerperium from lactation.

Management of diabetes and choice of delivery. The dietary management of diabetes in pregnancy consists in supplying the mother with enough calories to correspond with the rise of metabolism, which at term has probably increased 20 per cent, in providing for the baby's need for glycogen, and a division of meals which will insure the greatest protection against acidosis, glycogen depletion, and hypoglycemia. The special problems for each trimester must be considered separately.

The early nausea and vomiting of pregnancy can best be treated by hourly feeding and administration of insulin at three hour intervals. This of course may need to be supplemented by intravenous glucose. A safe diet would be carbohydrate 150, protein 60, fat 60 to 80 grams, and insulin every 3 hours—15 units if the Benedict test is red, 10 units if the

test is yellow or orange, and 5 units if yellow green.

The second trimester demands but little special care. The caloric and carbohydrate content of the diet should be increased. The problems of the third trimester are more baffling. By this time the baby needs 50 grams of glucose daily. The renal threshold is low and insulin must be increased cautiously. The basal metabolism is at its highest and the alkali reserve at its lowest level. Our diet averages carbohydrate 175 to 200 grams, protein 60 to 80 grams, and fat as needed. The urine should contain small quantities of sugar. Frequent blood sugar determinations will help to prevent hypoglycemia.

During normal delivery, the patient must receive 200 to 300 grams of carbohydrate. If a surgical delivery is chosen, the procedure is the same as at any operation—carbohydrate 100 grams by mouth or intravenously during the first 24 hours after delivery, and insulin every 3 hours according to the degree of reduction of the qualitative test for glucose.

Choice of delivery. The choice of delivery for the diabetic is debated. One must seriously consider the patient's background, the handicap of a chronic disease, a future in which the hazards of mortality and morbidity are greater than the average. There is also an economic hazard—periods of time when, because of illness, the diabetic is unable to perform her work, and her duties must be assumed by some one else; the extra cost of medical care, diet, insulin, and periodic health examinations. To the element of the mother's fear arising from normal pregnancy is the added element of fear of accidents to her child and to herself, because of diabetes. Her physical condition for the mechanical strain of labor is in inverse ratio to the duration of her disease, and in direct ratio to the control of her disease. Dr. Joslin has often said that to obtain the true age of our patients, we must add the duration of the disease to the chronological age. Thus a youthful diabetic at 25 years of age, the onset of whose disease was at 10 years—and this will be the problem of the future—is actually 40 years of age. Her disease has predisposed her to arteriosclerotic disease of the heart, eyes, and kidneys, to increased susceptibility to tuberculosis, possibly to depression of the hormonopoietic system, to anemias and damage of the liver, has made her muscles atrophic and poorly nourished, has predisposed her to degeneration of the peripheral nerves, and increased her susceptibility to infections with the colon bacillus and pyogenic cocci.

Prolonged difficult labor, normal or induced, has disadvantages for the diabetic. Those of immediate importance are the early exhaustion of the glycogen reserve and the danger of sepsis, the danger of hyperinsulinism, exogenous and endogenous, and the danger of acidosis. The secondary considerations are the added handicap of a torn perineum or cervix and consequent indication for later surgery. These patients are not physically fit for numerous pregnancies. The baby has not the vitality of the child of the non-diabetic, and great is the risk of injury from long labor to this large overdeveloped, but at the same time, flabby child. Furthermore, the induction of labor does not answer the problem as well as cesarean section because induction of labor is not safe until the cervix is soft, and the cervix may not be soft until after the baby has died.

Prolonged narcosis in the presence of low alkali reserve and glycogen depletion is a perfect setting for the onset of true diabetic coma. Everywhere it is evident that "the modern woman demands safe labor, freedom from unnecessary pain, a reasonable length of labor, and a complete restitution. . . ." In our opinion the diabetic deserves not less.

Outcome of pregnancies in patients with onset of diabetes in childhood. The very young diabetic, the onset of whose disease occurred in childhood, demonstrates to us even more than the older patients, that the pregnant diabetic requires accurate control of diabetes throughout pregnancy, an intimate association between internist and obstetrician, and double the supervision of the average pregnancy cases.

The maternal mortality in this group of 22 pregnancies in 15 mothers was high (Table VI). Two, who were not under our care at the time, died; 1 of eclampsia and 1 following a therapeutic abortion, making the maternal mortality for this special group 13 per cent in the insulin era. Of the pregnancies which came to

TABLE VI.—PREGNANCIES IN DIABETES WITH ONSET OF DIABETES IN CHILDHOOD

	Insulin	Duration of diabetes years	Onset age years	Date onset	Date pregnancy	Delivery	Outcome	Complications
1753	+		8	1916		Normal	Living birth	0
2124	+	12	14	1920	1932	Normal	Living birth	0
2847	+	13	9	1919	1932		Miscarriage	0
2776	+	11	8	1921	1932	High forceps	Stillbirth	Coma—pyelitis, arteriosclerosis
	+	12	8	1921	1933		Therapeutic abortion	
2802	+	12	14	1922	1934		Therapeutic abortion	Coma, death
3040	+	9	12	1922	1931	Normal	Living birth	Arteriosclerosis
4176	+	11	14	1922	1933	Forceps	Living birth	Puerperal sepsis
4506	+	5	14	1923	1928	Normal	Stillbirth	Arteriosclerosis
	+	7	14	1923	1930	Normal	Stillbirth	Arteriosclerosis
	+	7	14	1923	1930		Miscarriage	Arteriosclerosis
	+	8	14	1923	1931	Induced	Living birth	Arteriosclerosis
	+	10	14	1923	1933	Normal	Stillbirth	Arteriosclerosis
	+	11	14	1923	1934	Cesarean	Living birth	
6819	+	11	14	1922	1932	Induced	Stillbirth	Death—eclampsia
7014	+	14	14	1919	1933	Cesarean	Living birth	0
7251	+	10	13	1924	1934	Cesarean	Living birth	0
7407	+	5	14	1928	1932		Therapeutic abortion	
	+	6	14	1928	1934	Cesarean	Living birth	Sepsis
8256	+	6	14	1925	1931	Cesarean	Living birth	Toxemia
9903	+	3	14	1931	1934	Normal	Living birth	0
11563	+	2	15	1932	1934	Cesarean	Living birth	Eclampsia

term, 12 resulted in living births, and 5 in stillbirths. The incidence of stillbirth is thus five times that of the Johns Hopkins Hospital series of non-diabetics used as control. Miscarriages were not frequent, these occurred only twice (10 per cent). The incidence of eclampsia was 13 per cent and of non-fatal puerperal sepsis, among patients coming to term was 12 per cent. Two patients developed coma and 2 hypoglycemia. None developed a true gain in tolerance for carbohydrate. Two of the babies developed unexplained edema.

At the ages of 19, 22, and 23, 3 of the mothers had evidence of arteriosclerosis, 2 with demonstrable retinal hemorrhage, and 1 with peripheral sclerosis, demonstrable by X-ray.

Lactation. Lactation is poor perhaps because of relative undernutrition or lack of the specific lactogenic hormone. An analysis of milk of one diabetic patient showed nothing abnormal. None of our patients has been able to produce more than a few ounces of milk daily, when the diet has contained 2500 calories. Sherrill reviewed the literature on this subject and reported his own cases. Diabetic animals, as well as diabetic patients, fail to lactate normally.

Effect of diabetes upon the child. Congenital defects occur frequently in children of diabetic mothers. This is evident both in the series reported in the literature (8), and in our own patients. In our pre-insulin and insulin series of 166 babies, there were 7 abnormal. One was microcephalic, 1 a Mongolian idiot, 2 had congenital heart disease, 1 atresia of the gastro-intestinal tract, 1 achondroplasia, and 1 was a monster. The incidence of defects among stillbirths was 1 in 7, compared with 1 in 61 for consecutive cases at the Johns Hopkins Hospital, reported by Dippel. This included 1 diabetic. Two of the babies developed unexplained edema, 7 died in the first week, and 1 other died in the first year. Thus a 5 per cent mortality occurred in the first

year, which was exactly the mortality of the non-diabetic series reported by Peckam. Our neonatal mortality exceeded the control series slightly. The former amounted to 4 per cent and the latter 3 per cent. Thus it would appear that if a child of a diabetic mother is born alive, the life expectancy is good.

Inheritance. The problem of inheritance of the diabetic (39, 40, 10, 26, 27, 28) is indirect here rather than direct, for according to our present belief the potentiality for developing diabetes is inherited as a Mendelian recessive trait, and the child cannot inherit the disease from one diabetic parent alone, but only from two diabetics, a diabetic and a hereditary carrier or two hereditary carriers. The children of these diabetics, however, will all be hereditary carriers of the disease. Based upon an incidence of 0.3 per cent diabetics in the general population, we estimate that already 25 per cent of our entire population must be carriers of the disease, and such pregnancies increase the carrier incidence.

CONCLUSIONS

Premature delivery of the fully developed, though chronologically premature infant of the diabetic mother by cesarean section is the obstetrician's successful answer to the challenge. The cause and cure of the overripening of the fetus remain in the speculative stage, but the study of the hormones in diabetes offers hope for the correct solution.

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COMPOUND COLORED ALCOHOLIC SOLUTION OF MERCURIC CHLORIDE FOR SKIN DISINFECTION

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WE have been studying various solutions used in surgical practice for disinfecting the skin. The *in vitro* disinfecting powers of most of these solutions are satisfactory. Tinker and Sutton have reviewed the *in vivo* disinfecting power of several commonly used skin antiseptics. Some were found to irritate the skin. All of these solutions are too expensive. We have made up more than a hundred different solutions and studied various properties of each. Our object was to make up a solution that would possess the following properties: (1) a high phenol coefficient; (2) the power to penetrate the skin; (3) the power to remove fat from the skin; (4) a color so as to define the operative field; (5) the ability to lose the color promptly after operation; (6) it should not irritate, blister or burn the skin; (7) it must be inexpensive.

The bacteriological technique used to determine disinfecting power and phenol coefficients was carried out according to the recommendations set forth by the U. S. Department of Agriculture (1). The tinctures and aqueous solutions of various disinfectants used in the tables in this paper for comparison with our new solution are the same as contained in the *New and Non-official Remedies*.

The formula we have developed in our laboratory is given in Table I.

TABLE I.—FORMULA FOR ONE LITER OF THE COMPOUND COLORED ALCOHOLIC SOLUTION OF MERCURIC CHLORIDE

	Amount	Per cent
Ethyl alcohol (95%)	525 c.cm.	50
Acetone U.S.P.	100 c.cm.	10
Mercuric chloride	1 gm.	1:1000
Hydrochloric acid	7.5 c.cm.	0.75
Chrysoidin Y	2 gm.	1:500
Distilled water	367.5 c.cm.	
Total amount of solution	1000 c.cm.	

Alcohol. Alcohol lowers surface tension and is of itself a disinfectant. The penetration of dissolved mercuric chloride is facilitated and some defatting effect is obtained by using alcohol. We have varied the alcohol content from 10 to 80 per cent. It was found that 50 per cent alcohol was satisfactory. Lower alcohol content showed a rapid decrease in the disinfecting power. Higher alcohol content than 50 per cent showed some increase in disinfecting power but not enough to warrant the additional expense.

Acetone. Vaseline was rubbed into the skin. All excess was wiped off with dry gauze. Varying concentrations of acetone in 50 per cent alcohol were used to defat the skin by surface rubbing as is usually carried out in preparing the skin for surgical operative procedures. A drop of water was put on the prepared skin area to test the defatting effect. If the water spread uniformly into a thin layer, we considered the skin free of vaseline. Ten per cent acetone was the smallest amount we could use to satisfactorily defat the skin.

Hydrochloric acid. The H-ion is a good disinfectant. We have found that if sufficient hydrochloric acid was added to obtain the acid-disinfecting action, there was a burning sensation after application. Four per cent hydrochloric acid has been used in many of our solutions. This enhances the disinfecting power, but the solution was objectionable as already mentioned. We have used the amount of hydrochloric acid which was found to increase the disinfecting power of the mercuric chloride by increasing the ionization and hence making more mercury-ions available. We chose 0.75 per cent hydrochloric acid as the amount best suited for a non-irritating skin disinfectant. Table II gives a typical protocol of such an experiment.

Dye or coloring material. We were desirous of obtaining a dye which would color the skin in such a way as to clearly define the field treated with the skin disinfectant. The dye should not be of such a color as to subconsciously indicate hyperemia, passive conges-

TABLE II

Mercuric chloride 1:1000, alcohol 50 per cent and acetone 10 per cent was used as our stock solution. Varying amounts of hydrochloric acid were added to this stock solution.

Hydrochloric acid (per cent)	Highest dilution killing in 10 minutes
0.0	1:20,000
0.1	1:20,000
0.2	1:20,000
0.3	1:20,000
0.5	1:22,000
0.7	1:25,000
0.8	1:25,000
1.0	1:25,000
4.0	1:40,000
6.0	1:50,000

TABLE III

The highest dilution necessary to kill Staphylococcus aureus (No. 209 strain) in 10 minutes but not in 5 minutes at 20 degrees C.

Alcohol-acetone solution of: (suspended in 3 A's)	Highest dilution	Phenol coefficient
Chrysoidin Y, 2%	1:250	3.6
Mercurochrome, 2%	1:140	2.0
Phenol	1:70	1.0

TABLE IV

Highest dilution of disinfectant killing Staphylococcus aureus in 10 minutes but not in 5 minutes at 20 degrees C.

Disinfectant	Highest dilution	Phenol coefficient
Compound alcoholic solution mercuric chloride colored	1:25,000	357
Tincture of iodine	1:9000	128
Tincture of metaphen	1:4000	57
Tincture of merthiolate	1:6000	85
Tincture of mercurochrome	1:120	1.8
Phenol	1:70	1.0

TABLE V

Highest dilution of aqueous solutions of disinfectants killing Staphylococcus aureus in 10 minutes but not in 5 minutes at 20 degrees C.

Disinfectant	Highest dilution	Phenol coefficient
Mercuric chloride 1:1000	1:13,000	186
Mercuric chloride 1:1000 Hydrochloric acid 1%	1:18,000	257
Metaphen	1:10,000	143
Merthiolate	1:4000	57
Mercurochrome 3%	1:33	0.5
Phenol	1:70	1.0

tion or any other abnormal circulatory or system reaction. The dye should disappear from the skin within a day after its use. We used 85 different dyes in our work. Chrysoidin Y has proved most satisfactory in our hands. The color of the skin resembles that of tincture of iodine. The color gradually fades and disappears within 24 hours after applicafion.

Chrysoidin Y is not readily soluble in water but is soluble in alcohol, hence it was thought best to test its germicidal power in an alcohol acetone solution. We prepared these solutions according to the method outlined by Scott and Hill. Two per cent solutions were made up in 50 per cent alcohol, 10 per cent acetone, and 40 per cent water. Table III gives the results of our tests with chrysoidin Y and mercurochrome in dilutions necessary to kill Staphylococcus aureus in 10 minutes but not in 5 minutes at 20 degrees C. Chrysoidin Y was found to give a slight precipitate in the solution after standing several days. We were informed by the National Aniline and Chemical Company that the usual product contained 15 per cent impurities. They purified a sample containing 95 per cent chrysoidin Y and 4 per cent moisture. No precipitate is formed when this purified dye is used.

We were surprised to find the tinctorial material we had chosen possessed of itself a definite disinfecting power.

The relative disinfecting power of this compound colored alcoholic solution of mercuric chloride in comparison with other alcoholic solutions of disinfectants. Table IV summarizes the results we have obtained.

Aqueous solutions of various disinfectants were also compared. We used aqueous solutions of mercuric chloride and mercuric chloride with 1 per cent hydrochloric acid in water. Table V summarizes the results of these studies.

The formula we have used has been developed under controlled laboratory conditions. The solution was kept in tightly stoppered containers. We realize the skin disinfectant used in routine surgical practice would not be handled in this manner. We have, therefore, modified the constituents of this solution to facilitate ease of preparation and to allow for evaporation when placed in open vessels and re-used. The formula we suggest for practical purposes is as follows:

Ethyl alcohol (95%)	600 c.cm.
Acetone (U.S.P.)	200 c.cm.
Mercuric chloride	1 gm.
Hydrochloric acid (concentrated)	10 c.cm.
Chrysoidin Y	2 gm.

Make up to 1000 c.cm. with water.

We prepare this new compound colored alcoholic solution of mercuric chloride for one dollar and sixty cents per gallon in our laboratory. If large quantities of ingredients are purchased, the price would be lower. Tincture of iodine (U.S.P.) costs approximately four dollars and two cents and 3 per cent tincture of iodine costs us two dollars and sixty-five cents per gallon. The prices quoted us from various sources for tinctures of metaphen, merthiolate, and mercurochrome were over twenty dollars per gallon.

This new compound colored alcoholic solution of mercuric chloride has been used as the disinfectant in 300 cases of gunshot, automobile accidents, and other similar emergency hospital cases. It has been used in 120 cases of neck surgery and 65 cases of abdominal surgery. The reports are favorable, no infections followed, and the non-irritating properties of this disinfectant were commented upon by the surgeons using the solution.

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THE EARLY DIAGNOSIS OF CHORIOEPITHELIOMA[1]

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BEFORE the discovery of their pregnancy test by Aschheim and Zondek, the diagnosis of chorioepithelioma usually rested on the presence of profuse uterine bleeding, extensive metastases, and the finding of the tissue in the curettings. Now, however, since chorioepithelioma can be demonstrated by a positive pregnancy test, it appears that the diagnosis can be made early, even before metastasis takes place and with a considerable degree of certainty by the judicious use of the Aschheim-Zondek or the Friedman test. Early diagnosis is the *leitmotif* of this paper.

Mazer and Edeiken recently made a plea for the use of the Friedman test in cases of suspected chorioepithelioma because of the inadequacy of uterine curettage in the diagnosis, and these authors cite cases stressing the unreliability of curettage in the early diagnosis of the disease. Inspection of the pathological specimen in our first case proved to us conclusively that curettage could not have aided in the diagnosis; in fact, we would have been grossly misled by this procedure. We feel that diagnosticians should go one step further and follow every case of hydatid mole with pregnancy tests. Mazer and Edeiken came to the conclusion, which we think well founded, that abnormal uterine bleeding occurring within a few months after a mole pregnancy should not be treated by irradiation on the assumption that the bleeding is of the so-called functional type. We condemn the promiscuous use of radium in uterine bleeding at the cost of keen and finished diagnosis.

In the discussion of the paper by Mazer and Edeiken, Longaker cited a case which had been under his care for about 18 months in which a positive diagnosis of chorioepithelioma had been made because of the persistently positive Friedman test. However, his case remains unproven since, in the absence of clinical evidence, he did not operate on this woman and she made a perfect recovery. Since our first patient offered no clinical evidence at the time of the operation, we are in a philosophic mood as to whether or not these growths sometimes regress. This is a very interesting point and apparently no one can know whether such regression will take place or not. It is barely possible that she had such a tumor and that regression would have taken place eventually. In the discussion of the same paper, Hoffman elaborated some very interesting ideas. We quote his statements verbatim:

> The Aschheim-Zondek reaction is undoubtedly a most important adjunct in the diagnosis of chorioepithelioma. For purpose of prognosis, however, its value is less certain. Clinically and histologically, it is almost impossible to differentiate between the benign and the malignant forms of this condition. Both may give a similar clinical picture and either may give rise to metastases. Indeed, some authorities believe that these two forms are identical and that the outcome of the case depends upon the amount of antitrophoblastic agents present in the host. Since the Aschheim-Zondek reaction is positive for both forms, it fails to aid in the task of differentiation, and we remain, as before, dependent upon the occurrence of death for the determination of what form it is with which we have been dealing.
>
> Under the circumstances, therefore, it would seem best, before undertaking any radical procedure, to consider all factors, clinical and otherwise. The mere fact that a positive reaction has been obtained is not sufficient to justify such procedure. Emphasis should be rather placed upon the clinical evidence, especially when we recall that as yet it has not been established that a negative reaction rules out chorioepithelioma.

With due regard for the opinion of Hoffman, we cannot believe that it is justifiable to wait for metastasis in the face of persistently positive pregnancy tests before the operation is done, nor do we believe that we should temporize in the face of persistently positive pregnancy tests when we are sure that there is not a normal pregnancy in the uterus. Following this doctrine, some operations might be done needlessly, but the common good would be served. Whether or not a negative

[1] Read at the meeting of the Pacific Coast Society of Obstetrics and Gynecology, November 22, 1934, at Del Monte, California, and at the meeting of the Pan-American Medical Association cruising to Rio de Janeiro on S. S. Queen of Bermuda, July, 1935.

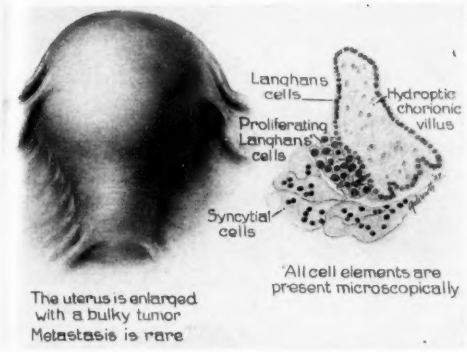

Fig. 1.

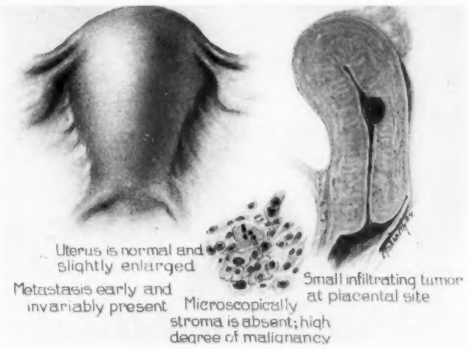
Uterus is normal and slightly enlarged
Metastasis early and invariably present
Microscopically stroma is absent; high degree of malignancy
Small infiltrating tumor at placental site

Fig. 2.

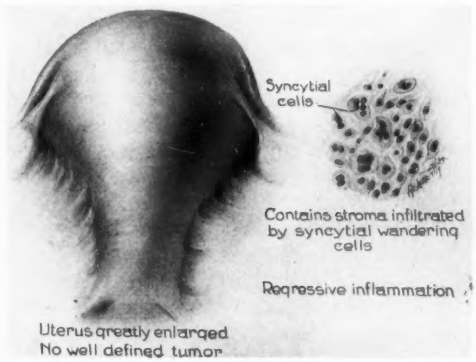

Fig. 3.

Figs. 1, 2, and 3. Artist's drawings showing the physical and microscopic characteristics of Ewing's three types of chorioepithelioma. Fig. 1. Chorioadenoma (follows mole). Fig. 2. Choriocarcinoma—follows labor, abortion, and ectopic pregnancy, missed abortion, and mole. Fig. 3. Syncytial endometritis.

reaction rules out chorioepithelioma, time and recorded study alone will determine. This fact and many others pertinent to the subject can be ascertained by following the dictum of Mazer and Edeiken that all cases of suspected chorioepithelioma should be checked by repeated Friedman tests and by following our further suggestion that all cases of hydatid mole be checked by the Friedman test.

There is a difference in response to ovary stimulating substances in rabbits of different ages. We noted in an early paper that follicle maturation and hemorrhage into follicles does occur in the rabbit ovary spontaneously in the absence of pregnancy, intercourse, or other known forms of artificial vaginal stimulation. We have never observed this ovarian activity in an animal younger than 4½ months of age. This activity must not, however, be confused with ovulation. It is certain that older animals are more susceptible to slighter degrees of stimulation than are the younger ones, and it is our contention that the few false positive Friedman pregnancy reactions reported by other observers must be due to the presence of those unruptured hemorrhagic follicles that do occasionally occur in rabbits older than 4½ months. In our series of nearly 400 Aschheim-Zondek tests and over 800 Friedman tests, we have less than 1 per cent false positive reactions.

We use animals at about 14 weeks of age, putting the upper and lower age limits at 12 to 18 weeks.

All of our specimens of urine are treated with toluol as soon as they are received. Decomposition and bacterial growth are prevented by this treatment. Saturation of the urine is accomplished with 2 drops of toluol to 1 ounce of urine. When a specimen arrives which is several days old, and which appears decomposed, it is easily detoxified by shaking with toluol and filtering through ordinary filter paper. It should not be injected until it is free from the putrefactive odor. More than one shaking with toluol and more than one filtering may be necessary, but this treatment does not seem to affect the accuracy of the test. Cloudy and foul smelling urine should always be treated in this manner. If this procedure is carried out routinely, the mortality of animals will be reduced to a minimum. We

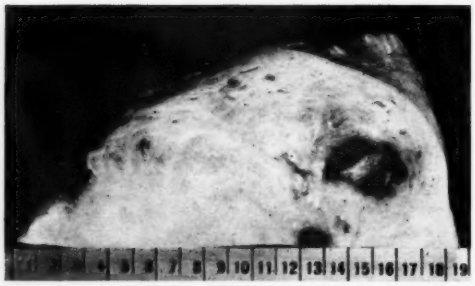

Fig. 4. Transection of uterus showing hematoma-like area of chorioadenoma. Case 1.

have found it advisable to treat fresh, clear urines in the same manner before they are used so that in case of question arising later, the same specimen is on hand. We have determined the reaction of over 400 specimens to litmus and have found that the reaction has no effect on the accuracy of the test. In experiments with the Friedman test we have obtained a good strong pregnancy reaction in a mature rabbit with 1 cubic centimeter of morning urine from a woman 5 months' pregnant. One cubic centimeter of the same specimen, injected into a 12 weeks' old rabbit of the same variety (New Zealand white) did not produce a reaction within 48 hours that could be called positive. Grossly there is evidence of follicle stimulation, but no evidence of hemorrhage into the follicles or ovulation. Either hemorrhage into the follicle or ovulation is evidence of a positive pregnancy reaction in an immature rabbit.

Aschheim and Zondek biologically assayed the gonad stimulating hormone in the urine of pregnant women and found that in normal pregnancy the kidneys excrete from 3,000 to 6,000 mouse units of hormone per liter during pregnancy, the peak being reached at the end of the fifth month of gestation. After this the quantity lost through the urine gradually diminishes.

On a weight for weight scale the ratio of a mouse unit to an immature rabbit unit of gonad stimulating hormone should be 225 to 1. Actually, however, this is not the case. As estimated by biological assay in immature female rabbits, we found that the kidneys excrete from 80 to 1,000 rabbit units per liter of fresh morning urine as estimated by the least amount of urine capable of producing detectable intrafollicular hemorrhage in 48 hours. As a matter of fact, an adult female rabbit weighing more than three times as much as an immature rabbit will show a positive pregnancy reaction with a smaller amount of urine than that required for a test mouse, thus giving evidence that a mouse unit is no less, and possibly greater than an adult rabbit unit of gonad stimulating substance. It must be kept constantly in mind that for most procedures other than qualitative ones, the rabbit is a notoriously unreliable laboratory animal, and the question of determining the unity of gonad stimulating substance by it is, at best, widely variable.

From these facts it seems certain that the differential diagnosis of normal and pathological pregnancy by a 1:10 dilution of the patient's urine, as advocated by Aschheim and Zondek in their original technique with mice cannot hold for the Friedman technique if mature rabbits are to be used. Although we carried out dilution procedures in only one of our cases of chorioepithelioma, it seems reasonable that a strong positive pregnancy reaction produced by 1 cubic centimeter or less of urine (1:10 dilution or greater) is indicative of an abnormally increased excretion of pituitary-like hormone in the urine, only if the animal used is immature.

What we mean to say is that while the fundamentals of the Aschheim-Zondek and the Friedman test appear to be the same, nevertheless the results obtained in testing a given urine might be different in mice, rats, immature rabbits, and mature rabbits. Dabney and Dabney have discussed this point in their work on the "Friedman Test in Hydatid Mole." However, they speak of Aschheim-Zondek as using rats, which is erroneous, and they failed to differentiate between mature and immature rabbits in their Friedman test.

We are thoroughly convinced that of the 4 animals, guinea pigs, rabbits, rats, and mice, the mouse is the only animal for the practical quantitative determination of pituitary-like hormone excretion in the urine. The rabbit and guinea pig are grossly unreliable and expensive. The follicular development in the

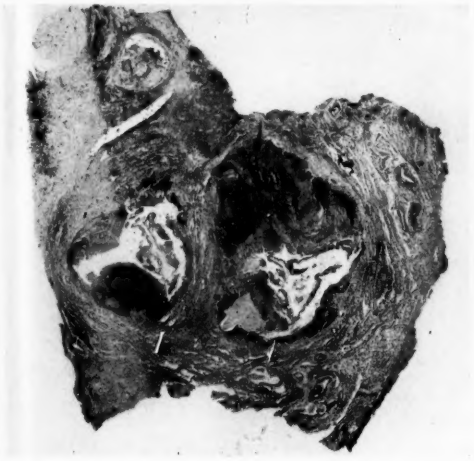

Fig. 5. Low power photomicrograph showing chorioadenomatous area near the interstitial portion of oviduct. Case 1.

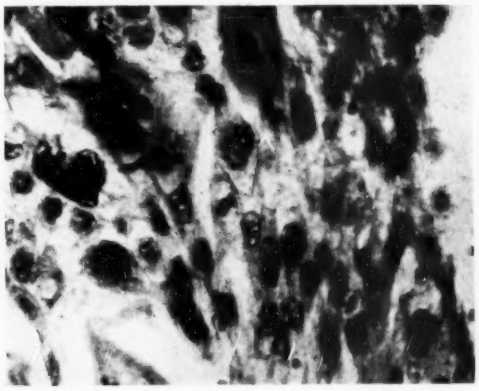

Fig. 6. Photomicrograph showing proliferating hyperchromatic Langhan's cells. Note mitotic figure near the center of the photograph and the syncytial cells in the upper edge. Case 1. × 375.

rat's ovary is a gradual one and preceded by a very short stationary phase. In the mouse, ovarian activity occurs more abruptly and there is a stationary phase before activity begins, during which phase the ovaries are very susceptible to follicular stimulation.

We have not carried out urine dilution tests completely on adult rabbits. Dabney and his associates have reported a positive pregnancy test in an adult rabbit (weight 3,722 grams) using 0.4 cubic centimeter of urine. A diagnosis of mole was made on this test, but the patient subsequently delivered a 5½ months' dead fetus with membranes intact.

In one of Siegmund's cases of chorioepithelioma, he reports a positive Aschheim-Zondek test using 0.005 cubic centimeter of urine in a mouse, or an equivalent of 200,000 mouse units per liter. This represents a prolan excretion of more than thirty-three times that which Aschheim and Zondek put as the upper limit for normal pregnancy.

Bishop has reported that the equivalent of one-three-hundredths cubic centimeter of urine injected into an adult rabbit may give a positive reaction in a case of chorioepithelioma.

Fahlbusch reports a case in which the diagnosis of chorioepithelioma was made from the curettings of the uterus. The Aschheim-Zondek test was negative. Because of the patient's ardent desire for children, expectant treatment was followed and subsequent tests were also negative. The patient is alive and apparently normal in every respect at the present time. This appears to be the only case on record where an Aschheim-Zondek test was negative in the presence of a chorioepithelioma. However, the urine for the first test was collected 5 days after the operation, and it is conceivable that the entire growth had been removed by curettage. In both of our cases the Friedman test was negative 5 days after removal of the growth by hysterectomy.

Since it is a fact that some chorioepitheliomas regress, while others are extremely malignant and cause death, it is hoped that an effort will be made to classify these tumors with respect to their malignancy and that a method of determining the malignancy of a given tumor by means of hormonal study might be devised. This has been done with a considerable degree of success by Ferguson in his cases of teratoma of the testes, and it appears to us that Ferguson's work might be duplicated in cases of chorioepitheliomas.

It has been rather disappointing, in our study of the literature of chorioepithelioma, that so few authors have made an effort to classify these tumors. We appeal to our readers to make a classification of these

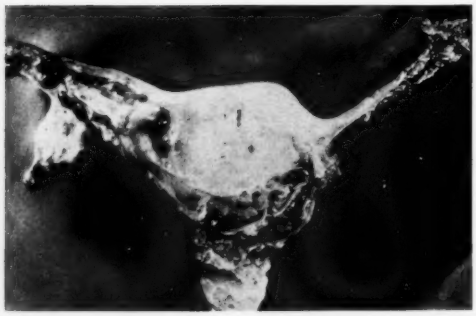

Fig. 7. Gross photograph of the entire uterus. both oviducts and the right ovary. Note the hematoma of right broad ligament and the hemorrhagic area along the left lateral aspect. The uterus is enlarged and asymmetrical. Case 2.

Fig. 8. The left half of the uterus sectioned transversely at intervals of 2 centimeters in five blocks. The upper cut was taken transversely through the hematoma on the right side of the uterus. Block 1, at the extreme right of photograph, note the hematomas. Block 2, note ragged cystic appearance of neoplasm. Case 2.

tumors and suggest as the best classification that of Ewing. The following is Ewing's classification:

1. Chorioadenoma (follows mole).
   a. The uterus is enlarged with a bulky tumor.
   b. Metastasis is rare.
   c. All cell elements are present microscopically.
2. Choriocarcinoma (follows labor, abortion and ectopic pregnancy, missed abortion and mole).
   a. Uterus is normal and slightly enlarged.
   b. Small infiltrating tumor at the placental site.
   c. Metastasis early and invariably present.
   d. Microscopically stroma is absent; high degrees of malignancy.
3. Syncytial endometritis.
   a. No well defined tumor.
   b. Uterus greatly enlarged and contains stroma infiltrated by syncytial wandering cells.
   c. Regressive inflammation.

We have searched the literature for cases of chorioepithelioma in which the Aschheim-Zondek test or the Friedman test was used for academic purposes or in conjunction with the clinical history in making the diagnosis, and we have found 34 reported cases. Abstracts of these cases have been made, but lack of space compels us to give only a brief summary.

This summary of the literature reveals the fact that in 34 cases of chorioepithelioma, the Friedman or Aschheim-Zondek tests were used either academically or corroboratively. The details of some of the reported cases are vague and some facts have to be derived by inference. Our study of these cases reveals that at least 20 followed hydatid mole. Twenty-one showed metastasis or vaginal bleeding. In 13 there was either palpable enlargement of the uterus or pelvic tumors. Following the preliminary curettage, 14 cases were curetted after the symptoms of chorioepithelioma had become manifest, and, in 8 of these 14, the diagnosis of chorioepithelioma was made from the scrapings. One of the cases was a definitely atypical case in an 8 year old girl.

As far as we can ascertain from a study of the literature on the subject, our first case is unique. Following the curettage for the removal of the hydatid material, the patient was *absolutely free from symptoms*. There was no more bleeding, her blood count increased, the uterus and pelvic contents were normal to palpation, she was in good health, free from complaints, and had gained weight. There was no cough or any sign of lung involvement. The sedimentation rate remained slightly increased and the Friedman test was persistently positive. In all other cases reported, there was bleeding, signs of metastases, enlargement of the uterus, or some other signs of chorioepithelioma. Our case is extremely interesting because we have been able to follow so well the continuity of the progress through pregnancy and hydatid mole, chorioepithelioma and eventual cure. The interest is increased because the opportunity to make such an early diagnosis and remove so small a chorioepithelioma so rarely comes in one's life. The free use of the Friedman test has revealed the sequence of events before and after operation in a spectacular manner.

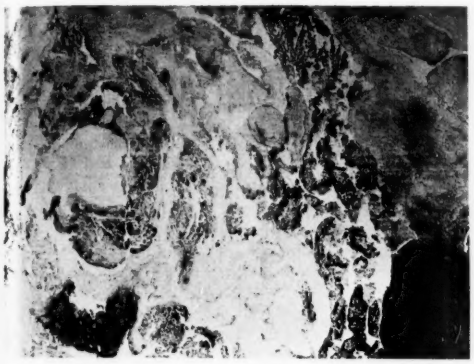

Fig. 9. Low power photomicrograph showing cellular zone of choriocarcinoma in the region of the broad ligament. Case 2.

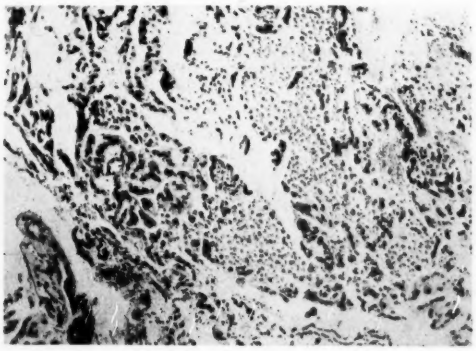

Fig. 10. Photomicrograph illustrating the admixture of proliferating and invading Langhan's and syncytial cells of choriocarcinoma. Case 2.

CASE 1. Mrs. W. A., aged 30 years, consulted one of us (A.M.) May 9, 1932, complaining of sterility after 4½ years of marriage. Her appendix had been removed, and her only other complaints were those of severe cramps on the first day of her menstrual period and dyspareunia caused by vaginismus. Her physical examination was negative, except that her uterus was somewhat smaller than normal, sharply antiflexed, and pulled to the right. An hysterosalpingogram showed a stenosis of the internal os, complete filling and patency of the right tube, and no filling of the left tube. There were some filling defects in the contour of the fundus which suggested hyperplasia of the endometrium. The stenosis of the internal os was dilated and the uterus was curetted. The pathologist's report on the curetting was as follows: This tissue has the appearance somewhat suggestive of menstruating endometrium, and there is nothing suggestive of malignancy, unusual hypertrophy, or hyperplasia.

The patient returned home shortly after this operation. She menstruated once—the last week in May—just 1 month after the period in April. She missed the June period, wrote to that effect, and a specimen of urine was requested. The Friedman test with this urine was positive just 9 days after the missed period.

On July 20, because of the recurrent vaginal bleeding, which had started July 3, the patient came to Portland and was put in the hospital for 10 days. The Friedman test at this time was positive. She bled, more or less, during these 10 days and, deeming that she was having an abortion, on July 29, we had about decided to curette the uterus when a Friedman test reported on that day was found to be positive. We became suspicious of hydatid mole, and on two occasions the patient was examined with a speculum and her pads were examined for traces of vesicles. None, however, were found. As the bleeding gradually ceased, she was allowed to return to her home and was referred to a local physician.

A specimen of urine on August 13 showed a positive reaction. On October 5, her husband wrote that during the previous months there had been no enlargement of the uterus, that there was a slight bloody flow every night, daily morning nausea, but no cramping pains. Late in October her physician notified me that on October 25, the patient had passed an hydatid mole surrounding a fetus which apparently had ceased to develop when about 3 months old. A few days after this we were notified by the patient that she was still bleeding considerably, and we ordered another specimen of the urine which, on November 10, gave a positive Friedman test. We sent for the patient, and she came to Portland on November 15, and the uterus was curetted on November 16. The curettage revealed considerable débris containing many hydatid vesicles. During the curettage there was an alarming uterine hemorrhage, and the uterus was immediately packed tightly with gauze. The pathologist's report of the scrapings was: hydatid mole with moderate Langhan's cell and syncytial cell proliferation.

There was absolutely no bleeding during the stay of the patient in the hospital following the curettement, and she returned home on November 24. From this time on there was no uterine bleeding whatever, but on December 12, and on December 27, the Friedman tests were still positive. The positive Friedman tests without bleeding made me quite certain that, while there was nothing left of the mole, which involved the endometrium, there were two contingencies possible: either the mole had invaded the myometrium or a chorioepithelioma had formed.

The patient was again sent for and arrived on December 27. She was in good health, free from complaints, and had gained weight. There was no cough, nor any sign of lung involvement, and her red cell count had risen markedly since the curettage. The uterus was freely movable, normal in size and position, and there was nothing abnormal palpable

in the region of the adnexa. In other words, there was absolutely no clinical sign of chorioepithelioma. The patient was of high intelligence, and had studied the subject of mole and chorioepithelioma and agreed with me that the uterus should be removed.

On December 29, the abdomen was opened; the uterus was found to be slightly retroflexed with no enlargement, and was normal in every respect except for slight bulging of the posterior part of the fundus. Both ovaries were normal, except for a corpus luteum in the left ovary. There was no evidence of lutein cysts. A supravaginal hysterectomy was performed. The patient made an uneventful recovery. The pathological examination done by Dr. Thomas Robertson was as follows: Early chorioepithelioma (chorioadenoma type) of the left uterine cornu arising subsequent to penetrating hydatid mole. Degenerating hyalinizing chorionic villi which have penetrated into the myometrium; edema of the myometrium; fibrosis of the myometrium.

Sections of this growth were sent to James Ewing who corroborated the diagnosis as follows: "The sections show a typical example of that form of chorioma in which the villi are preserved and which some years ago I ventured to separate from other choriomas by calling it chorioadenoma. Another term is destructive placental polyp. Clinically it is less malignant than fully developed choriocarcinoma in which the villi are absent."

Following the operation, the patient made an uneventful convalescence. The Friedman test was positive on each of the 4 days following the operation, and the tests on the fifth, sixth, and seventh days following the operation were negative, so that we can say that in this case the hormone was present in the blood for 4 days following the removal of the uterus and after that was absent. The patient was discharged from the hospital and returned to her home 14 days after the operation.

In the following 8 months, the Friedman tests done in January, February, March, April, and July were negative. The patient's blood count was hemoglobin, 94, and red cell count, 5,600,000. The patient has gained several pounds in weight and is in perfect health now, over 2 years after the hysterectomy.

Case 2. Mrs. N., aged 19 years, was treated by a colleague (Dr. Loar) for threatened abortion, February 12, 1934. She apparently recovered but returned to the hospital again in 6 days with bleeding. She was at that time about 3 months' pregnant. The uterus, however, was increasing in size and had reached the size of a 7 months' pregnancy. On March 7, Dr. Loar emptied the uterus of an hydatid mole. A severe hemorrhage accompanied this operation. The patient recovered nicely but was anemic. The Friedman test was positive 2 weeks, 4 weeks, and 6 weeks after the mole had passed. On April 18, there was a severe uterine hemorrhage, necessitating packing of the uterus. The Friedman test, done every 2 weeks after the delivery of the mole, was positive up to the time when I saw her on June 5, 1934. At the time the hemoglobin was 64 per cent, and the red count 3,920,000. On examination there was extensive laceration of the cervix. The uterus was about twice its normal size and boggy. The Friedman test, using an immature rabbit, was positive at this time, with three-tenths cubic centimeter of urine; but was negative with one-tenth cubic centimeter of urine. X-ray of the lungs revealed no evidence of metastases. A complete hysterectomy was done on June 11, 1934. Both ovaries were free from cysts. Uterus was enlarged and boggy, and on each side, extending into the broad ligaments, were big, purplish-bluish masses, approximately 3 centimeters in diameter; and, on the right side, the mass seemed to extend along the round ligament. The tissues were incised well outside of these masses and a complete hysterectomy was done, including the right ovary, which was adherent to the right broad ligament. The patient made an uneventful recovery. The pathological examination done by Dr. Warren C. Hunter was as follows:

Choriocarcinoma of uterus with extension into veins of both broad ligaments, massive hemorrhage, and necrosis; corpus luteum of right ovary of the type seen in pregnancy; old laceration of cervix uteri.

The pathological diagnosis of Dr. Thomas Robertson in the first case, and that of Dr. Warren C. Hunter in the second case have been corroborated by Drs. John Ewing, Frank Lynch, and Frank Menne. Both patients are alive and well. The first, 2 years after her operation; the second, 7 months after her operation. The Friedman test in both cases has been negative since the fifth day following operation. No sign of metastases or recurrences in either case has been found to be present.

SUMMARY AND CONCLUSIONS

After a correlation of our cases with those cases reported in the literature as having been verified by a pregnancy test, we feel that our first case is extraordinary. A study of the details of the reported cases convinces us that no other case has been diagnosed and proven so early in the absence of symptoms. Our diagnosis rested entirely on two facts: the history of mole and the persistence of anterior pituitary-like hormone in the urine. We can classify our first case according to Ewing, only by a microscopic study of the specimen since the clinical findings do not correspond to those of Ewing's group. This fact may be due to the youth of our tumor.

As we consider our cases and those reported in the literature, several questions arise in our minds. Would the tumors found in our patient have regressed? Can there be a negative pregnancy test in the presence of a chorioepithelioma? The case reported by Fahlbusch appears to be the only one in the literature which might answer this question in the affirmative. However, since the pregnancy test was negative on the fifth day following his curettage, may we not assume that Fahlbusch had removed the entire growth with the curette?

Whether or not there can be a negative pregnancy test in the presence of chorioepithelioma can be determined only by critical observation of the results obtained in testing for the pituitary hormone in many cases of known chorioepithelioma. Will it not eventually be possible to foretell the degree of malignancy of a known chorioepithelioma by biological quantitative assay of the patient's urine?

The question of removal of the ovaries in conjunction with the hysterectomy for chorioepithelioma requires discussion. It is an acknowledged fact that in other forms of malignancy there will be less danger of recurrence if a thorough operation is done. However, it seems reasonable to believe that in cases of chorioepithelioma, diagnosed early, one need not remove the ovaries. As a matter of fact, in our first case only a supravaginal hysterectomy was done, and there was no evidence of extension or recurrence or metastases. In the second case, a complete hysterectomy was done because of severe lacerations of the cervix and the right ovary was removed only because it was firmly adhered to the posterior sheaf of the right broad ligament. Our patients were both young women, and it hardly seemed reasonable to remove ovaries that had all the gross appearance of being normal. The results in our 2 cases seem to have justified this procedure. It remains to be seen, however, whether or not this is good judgment. From our experience, we would assume that in operating for chorioepithelioma where the diagnosis has been made early and where the growth appears to be confined to the uterus, it would be good judgment not to remove the ovaries if they had all the gross appearance of being normal.

There is so much unknown concerning the anterior pituitary-like hormone and the fundamental physiologic facts concerning it, that it would be presumption on our part to be dogmatic on the subject. We feel, however, that in the light of our present knowledge, chorioepithelioma can be definitely diagnosed shortly after its inception. We wish to stress the point of early diagnosis. We feel that every patient who passes a mole should have her urine examined for anterior pituitary-like hormone by the Friedman test monthly for at least a year. In this way a developing chorioepithelioma might be diagnosed early and removed before symptoms appear or before metastases develop.

Here, then, are the reports of 2 cases of chorioepithelioma in which the diagnosis was made early by means of the Friedman test. The patients were operated on and cured; the first, 2 months and 4 days, the second, 3 months and 4 days after the passing of an hydatid mole.

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HYPEROSTOSIS FRONTALIS INTERNA

A Preliminary Study

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THE term hyperostosis frontalis interna was chosen to designate a peculiar and striking condition occasionally found in the frontal bone and associated with various symptoms which will be described. When this title was selected the writer was ignorant of the thesis of Ferdinand Morel, "L'hyperostose frontale interne. Syndrome de l'hyperostose frontale interne avec adipose et troubles cerebraux," published in 1930. It was only through search of the *Index Medicus* for the title "hyperostosis frontalis interna" or a similar one, that Morel's thesis was found. The name hyperostosis frontalis interna will be retained in this paper as it seems preferable to the French equivalent. However, there is no question as to priority in the selection of terms or presentation of the subject. To Ferdinand Morel all credit is due for his excellent study and the first report of a living example of the condition, which is to be discussed in this communication.

Radiological examination of the skull during some 10 or more years has on rare occasions shown a peculiar thickening of the frontal bone. This thickening has been considered as either a normal anatomical variation, such as overdevelopment of the groove for the longitudinal sinus, or of bone formation, or calcification in the falx cerebri, or some indefinite type of osteitis. The patients in whom it has been found have not had pathological study of the area in question or examination at autopsy. Little attention was paid to it. Nevertheless, the finding seemed significant, and its occurrence was more carefully noted for some years. In 1929, an example of melorheostosis came under observation and it was thought that this condition in the frontal bone might be a cranial manifestation of that disease. From then onward the cases having this change were carefully noted in the hope that a sufficient number would be collected to warrant a study of what was thought to be melorheostosis of the cranial bones. The cases were too infrequent in occurrence to result in any progress. Consequently, it seemed advisable to re-examine all the radiographic mate-

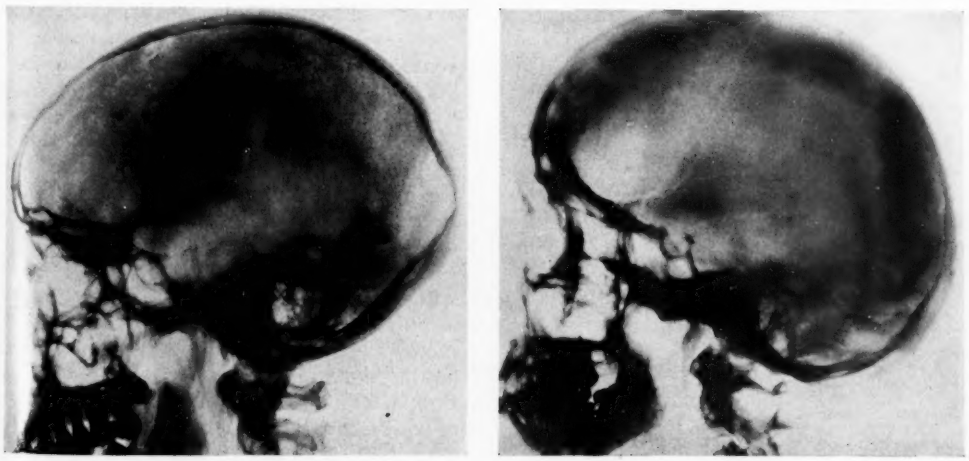


Fig. 1. Lateral roentgenograms of skull of normal adult individuals. Left, male. Right, female.

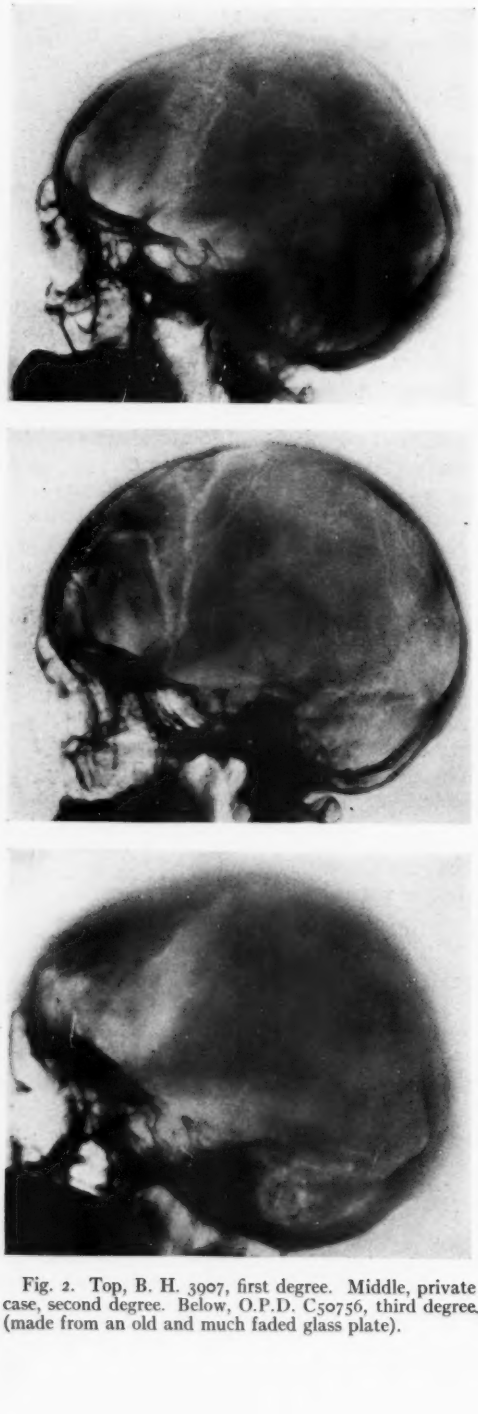


Fig. 2. Top, B. H. 3907, first degree. Middle, private case, second degree. Below, O.P.D. C50756, third degree (made from an old and much faded glass plate).

TABLE I.—AGE, SEX, RACE

Ages in years	Female		Male	
	White	Colored	White	Colored
0 to 10	329	24	507	31
10 to 20	383	35	491	28
20 to 30	522	62	537	51
30 to 40	455	62	499	55
40 to 50	368	37	479	46
50 to 60	240	15	330	17
60 to 70	99	2	180	3
70 to 80	25		36	
80 to 90	4		3	
Total	2425	237	3062	231

Females—45%
Males—55%

White—92%
Colored—8%

rial available. Before discussing the reexamination some remarks on the literature of the subject are in order.

The literature is fully covered by Morel and but brief reference will be made to it. His thesis, published in 1930, is based on 4 personal autopsies at the Bel-Air Asylum at Geneva, the protocols of 11 others and a study of a living case, at the time of his writing an inmate of the asylum. In 1930, Van Bogaert reported a case, "Le syndrome de l'hyperostose frontale interne chez une malade présentant par ailleurs un Cécité psychique par hémianopsie double," and in 1931, P. Schiff and J. Trelles recorded an additional case under this title, "Syndrome de Stewart-Morel. (Hyperostose frontale interne avec adipose et troubles mentaux)." As far as the writer is able to ascertain, these 3 cases are the only ones studied during life. However, the clinical aspects and radiological findings are so characteristic and unique that the disorder must have been described more frequently. If so, the reports are under titles difficult or impossible to find.

Hyperostosis of the frontal bone associated with obesity has been known in the autopsy room for an exceedingly long time. Morel relates the interesting fact that Morgagni and Santorini performed an autopsy on an old woman undoubtedly having hyperostosis frontalis interna, an observation published in 1765. Naito, in his monograph "Die Hyperostosen des Schaedels" includes the X-ray

examination of 9 skulls with hyperostosis, but little or no history. Casati, in 1926, "Die senilen Schaedelveraenderungen im Roentgenbild," published radiographs of 5 examples of the condition found among museum specimens. R. M. Stewart reported the autopsies of 3 personal cases and a study of certain museum specimens in 1928 under the title "Localized Cranial Hyperostosis in the Insane." D. M. Greig, in 1928, published an elaborate article "On Intracranial Osteophytes." His study was based on 188 crania in the Museum of the Royal College of Surgeons of Edinburgh. Among them were 32 with "intracranial osteophytes," many of them identical with those of hyperostosis frontalis interna. An interesting point is the fact that he states that the orbital portion of the frontal bone is free from the hyperostosis.

The radiographic material studied was that in the file of the Edward Mallinckrodt Institute of Radiology, which also contains the X-ray negatives of its predecessor, the X-ray Department of the Washington University School of Medicine. The roentgenograms were accumulated from September, 1911, to May, 1934. During that period there were 288,860 admissions to the Washington University Dispensary and its successor, the Washington University Clinics. There were, in the same period, 127,084 admissions to the hospitals allied to the Washington University School of Medicine, namely, the Barnes, the St. Louis Children's, the St. Louis Maternity, and the McMillan Eye, Ear, Nose and Throat Hospitals. The total number of patients applying to these institutions was 415,944 and roentgen examinations were made on 96,076 of them. Of these 5,955 were of the skull (Table I).

In the interest of accuracy and because the particular frontal bone change was either not noted or, if noted, done so under innumerable designations or synonymous terms, it was essential to review all X-ray negatives of the skull, from 15,000 to 20,000 in number. To insure complete mental detachment and to make the survey wholly objective in character, the plates and films were examined to determine whether or not there was deviation from the roentgenographic findings of a normal individual (Fig. 1). There was no prior knowledge of the history of the case, reason for the examination, or other facts concerning the patients. The negatives were reviewed in the order in which they were made. This method was essential for elimination of the natural tendency to find in an X-ray examination that which symptoms, physical examination, or other facts indicate should be present.

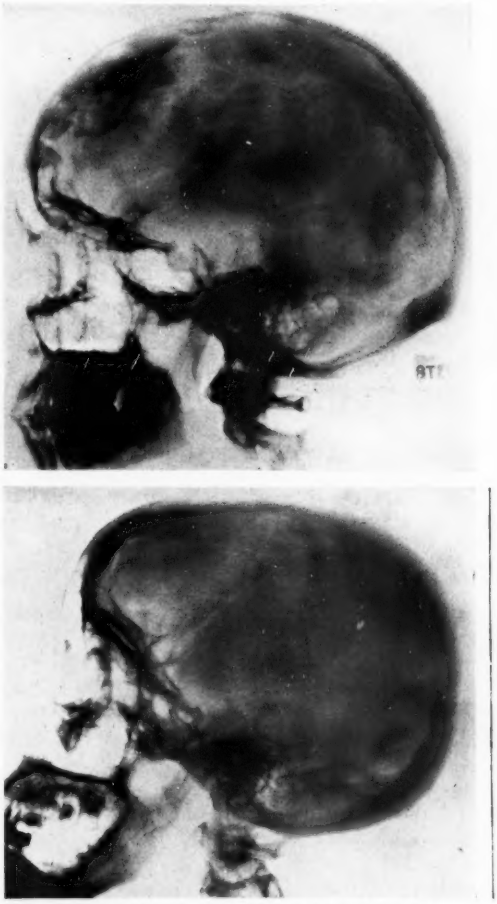


Fig. 3. B. H. 34347. Above, nodular type of hyperostosis. B. H. 173338. Below, sessile type of hyperostosis.

Practically all roentgenographic examinations of the skull were made stereoscopically in the lateral projection. Many had in addition a postero-anterior projection and many

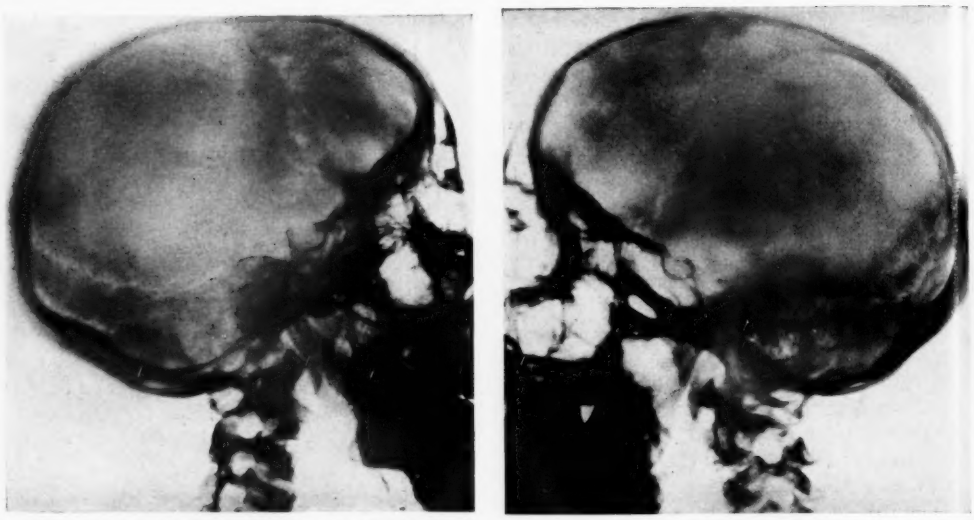


Fig. 4. B. H. 19239. Left, involvement of orbital plate and squamous portion of the frontal bone. Right, B. H. 1979, orbital plate alone involved.

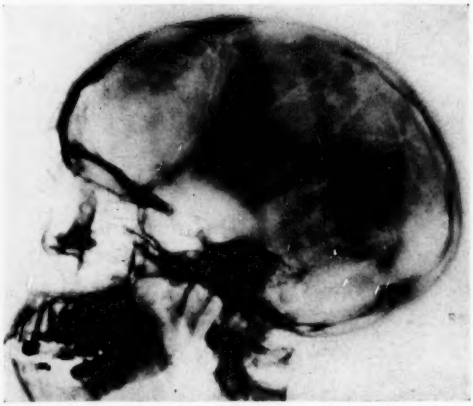
of the latter were also stereoscopic. Because of inefficient apparatus, poor technique, and the effects of time, many of the earlier plates and films had to be eliminated from consideration. If roentgenograms of other regions of the body had also been made, those were examined to ascertain if there were bone changes elsewhere. No such changes were discovered.

Seventy-two examples of frontal bone hyperostosis were found. They varied in degree from those in which the change was detectable to extreme thickness. It was impossible to consider the variation in thickness and density in relation to the time of existence of the bone change. The examples are divided into three classes, first, second, and third degree in ascending order (Fig. 2). They are of three types, nodular, sessile, and mixed (Fig. 3).

Regionally, the hyperostosis can be classified into that in which it is confined to the squamous portion of the frontal bone, to its orbital plate, and to a combination of the two (Fig. 4). The hyperostosis was associated in a few cases with hyperostosis elsewhere in the vault of the skull, notably an indefinite thickening of the frontal bone near the coronal suture lateral to the sagittal plane.

The hyperostosis is of a dense order, the density being disproportionate to that which could be ascribed to the increased *volume* of the involved portion of the bone. Though it may extend far up on the squama, it is not observed beyond the coronal suture. The frontal sinus may have its posterior wall thickened on the cranial aspect but the cavity is not decreased.

There is no evidence of hyperostosis of the sphenoid, temporal, or malar bones. The cribriform plate of the ethmoid is scarcely or not at all possible of roentgenographic examination, hence no statement regarding it can be made. It is to be remembered that the ethmoid is developed in cartilage, whereas the frontal is a membranous bone. The lateral extent of the hyperostosis is not determined even in the postero-anterior view. This region cannot be investigated with certainty by roentgenography because of superimposition of too many structures in the postero-anterior projection and the backward curvature of the lateral portion of the squama frontalis. The hyperostotic change gradually fades from the midline laterally. At the midline there is a narrow zone in which the hyperostosis is nonexistent, or is present to only a slight degree. In the living subject the thickness of the



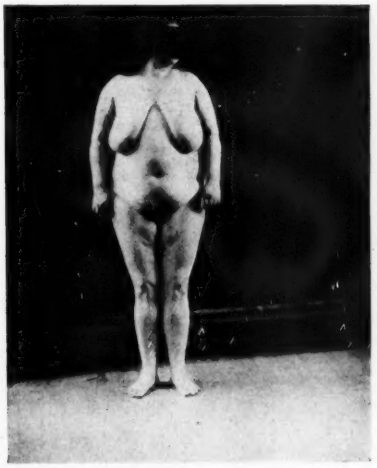


Fig. 5. B. H. 2788. First degree hyperostosis. Photograph illustrating obesity.

hyperostotic area can only be estimated in roentgenograms made in the lateral projection.

Schueller writes that "apart from variations in thickness in separate skull regions the average thickness of the skulls of different adults varies between 3 to 8 millimeters." Table II is an attempt at measurement of the hyperostotic areas; they were made at the extreme point of thickening. It must be remembered, however, that these are measurements of roentgenograms which are made at a point on the sagittal plane and outward over a curved surface and that they are of relative value only.

In no case was there any evidence of alteration of the outer table of the skull. The diploe, according to the degree of hyperostosis, is either diminished or obliterated, and this appears to be progressive. When the thickening reaches the inner aspect of the outer table, its progress is arrested and in such cases there is radiographically a homogeneous mass of dense bone extending from the outer surface of the skull to the inner limits of the hyperostotic zone. In the cases in which the orbital plate is involved, there is, of course, no replacement of diploe by compact bone, because the orbital plate is papyraceous. Toward the cranial cavity, the hyperostosis extends, in the most extreme case in the material which was studied, 46 millimeters from the outer surface of the cranium (see Fig. 2). The zones of hyperostosis are wavy in their intracranial outline in the nodular and smooth in the sessile type, and are homogeneous in texture. There are no signs of bone destruction or calcium loss. In all cases, the skull was free from evidence of increased porosity with one exception (B.H.24503). Since the hyperostotic area is radiographically, at least, formed of a mass of dense bone, it is necessary to compare it with the hyperostosis or hypertrophy which are to be observed in other bone dystrophies.

Through its physical characteristics, location, and incidence, this hyperostosis is distinct from that observed in the infectious processes of bone, primary or secondary bone tumor, osteitis deformans, melorheostosis and leontiasis ossea. It obviously should not be confused with those bone dystrophies in which porosity or calcium loss is a feature. It lacks all the characteristics of the bone changes observed in the blood dyscrasias.

Hyperostosis frontalis interna is the antithesis of those diseases which have a deficiency of skeletal calcium as a part of their picture. It is, therefore, a reasonable supposition that it is a disorder of calcium metabolism[1] in

[1] The term calcium metabolism will be used throughout this paper. It is to be understood that the term includes all related metabolites.

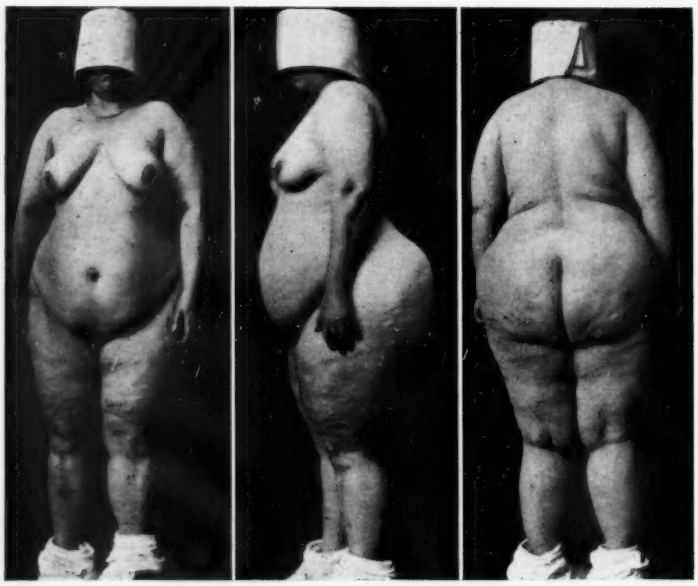


Fig. 6. B. H. 42710. Illustrating obesity.

which that mineral is present in excess in the organism. Greig and Morel are of this opinion. There is associated a disturbance of fat metabolism manifested as obesity which is at times extreme (Figs. 5, 6, and 7). The occurrence of the latter is less constant than the calcium disorder as it is seen in but 44 per cent of the cases.

The incidence of hyperostosis frontalis interna will vary with various types of institutions. In a general hospital and dispensary in a period of 23 years, there were 59 examples in 415,944 patients, a percentage of .014. In an X-ray laboratory 72 cases were found in 96,076 examinations, a percentage of .075. On roentgenographic examination of the skull alone there were 72 examples in 5,955 cases or 1.2 per cent. At the Bel-Air Asylum in Geneva, Morel found the incidence to be 1.4 per cent of the autopsies. Regardless of these percentages, it is a fact that the actual incidence must be higher than the figures mentioned; certainly it will be found so if the condition is sought for. The surest means of determining the existence of the hyperostosis is by radiographic examination. Certain degrees or types of hyperostosis may readily escape notice at autopsy.

After segregation and analysis of the roentgenographic material, the 59 cases in which a clinical history was available were analyzed. The case histories were reviewed in the same manner as were the examinations of the skull, that is, as far as was possible under the circumstances, with complete detachment. No reference was made to the radiographic findings and only the salient points in the histories were noted, or that which appeared to be of importance to the writer of the clinical record.

Analysis and tabulation of these facts in the histories are immediately arresting and are as striking as were the results of the review of the roentgenograms (Table III). The important features in the table may be summarized as follows: With two exceptions (B.H.25796 and B.H.26766) which were acute traumatic cases, 70 patients had neurological or neuropsychiatric symptoms of an intensity requiring a roentgenographic examination of the skull. Fifty-five, or 76 per cent, of the 72 cases were hospitalized, 97.2 per cent were females. Of

those 59 with histories available, only 50.8 per cent had been pregnant (from 1 to 21 times), 3.4 per cent had a positive Wassermann. The ratio of colored to white patients was approximately the same as that prevailing in this clinic, 62.7 per cent had headache, 5.08 per cent migraine, 8.5 per cent had convulsions, 44 per cent were obese, and 5 per cent had thyroid disorder. There is some justifiable doubt as to the two male cases being true examples of the disorder (Fig. 8). The incidence by decades is shown in Table IV.

There are certain impressions gained from the tabulation of the histories which cannot be put down in figures. The majority of the patients gave a long history of morbidity which is quite indefinite. There is no evidence that pregnancy or barrenness has any relationship to the condition. The reading of the histories of these cases individually leaves an impression of vagueness, the symptoms related or the physical examination do not fit with any particular pathological state or they might be a part of many diseases. Taken *en masse*, however, they constitute a definite syndrome which is distinctive. Polyphagia, polydipsia, polyuria, and disturbance of sleep emphasized as important symptoms by Morel were not recorded in 59 of the cases. Possibly these symptoms were so slight that they escaped notice.

If on X-ray examination of the skull, hyperostosis of the frontal bone is encountered, it is the most certain sign of the existence of this disorder, and one is tempted to refer to it as a "pathonomonic" sign. If

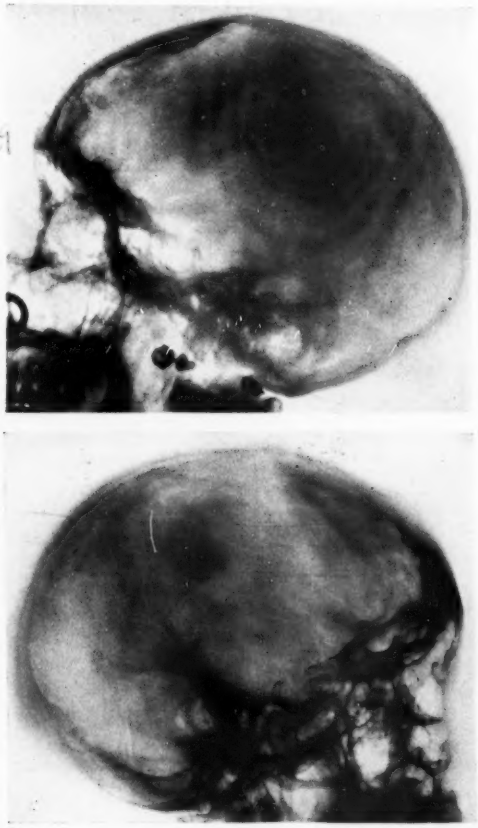


Fig. 7. Same patient as in Figure 6. Above, roentgenogram of skull in 1924. Below, roentgenogram of skull made in 1934. There is a question of slight enlargement of the sella turcica.

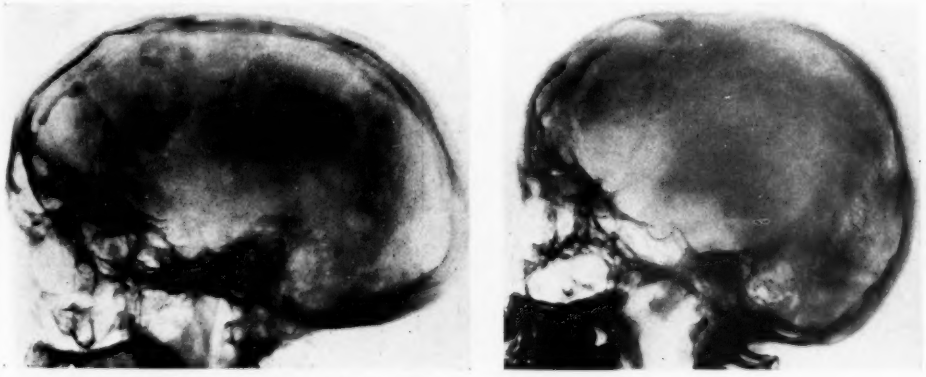


Fig. 8. Roentgenograms of the two male cases.

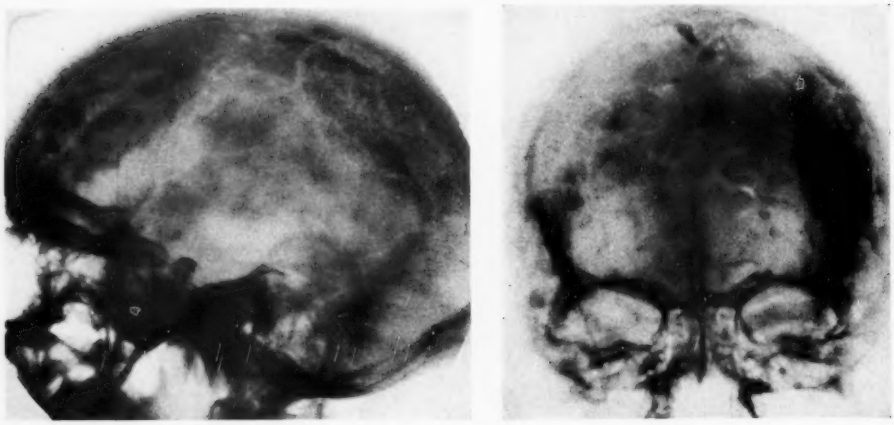


Fig. 9. B. H. 18072. Left, lateral roentgenogram. Right, postero-anterior roentgenogram of skull.

coupled with hyperostosis there is a tendency to obesity, various bizarre mental and neurological symptoms and signs, the diagnosis of the condition is established. In addition to this, the degree of the hyperostosis seems to be in relation to the intensity of the symptoms and both the hyperostosis and the symptoms appear to be of a progressive nature. There must be a single fundamental cause which produces both the hyperostosis and the symptoms from which the patients suffer in the beginning. At a later period if the hyperostosis is of such an order that the cranial contents are encroached upon by bony overgrowth, there are superadded other symptoms which are not to be confused with those traceable to the unknown fundamental causative factor. To illustrate, autopsy reports in the extreme degrees of hyperostosis mention the fact that the frontal lobes conform or are molded to the hyperostotic zone. This can only mean that the brain atrophies before the advance of the encroaching bone. Naturally in such cases what is being dealt with is cerebral pressure analogous to that of a long standing depressed fracture of the skull.

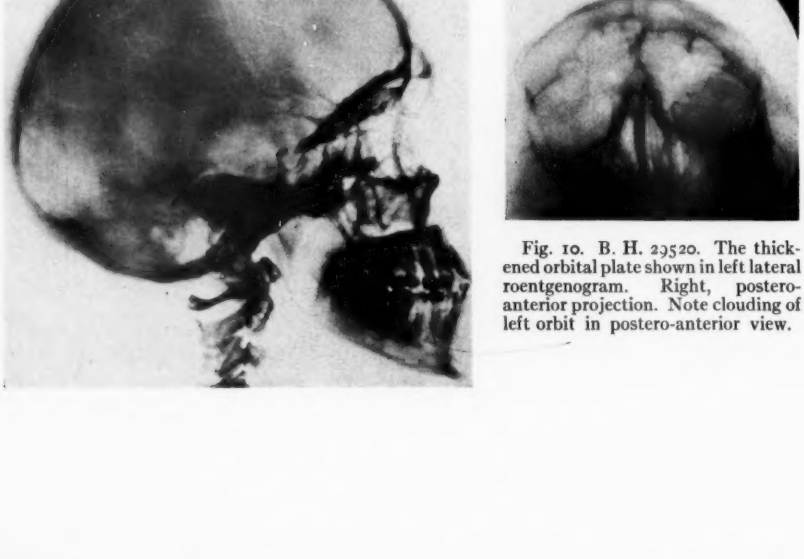


Fig. 10. B. H. 23520. The thickened orbital plate shown in left lateral roentgenogram. Right, postero-anterior projection. Note clouding of left orbit in postero-anterior view.

There have been no convincing roentgenograms which demonstrate hyperostosis throughout the base of the skull except in the case of the orbital plate of the frontal bone. Nevertheless, the high incidence of seventh and eighth nerve symptoms, strongly suggest that hyperostosis of the temporal bone may be the cause of the symptoms, frequently found, referable to these nerves. Morel's case (Case No. 11) had isolated hyperostoses on the petrous portion of the temporal bone.

It is impossible to understand why there is a selectivity of location of this hyperostosis. The assumption that there is a selectivity must be provisional until it has been established by autopsy and roentgenography that there is no accompanying hyperostosis of the other portions of the skeleton. Greig's view is that the senile skeleton (the average age of his cases was 70 years) because of general inactivity of elderly individuals, loses its calcium to the blood stream. In consequence of this there is calcium retention which is deposited somewhere in the organism. In the case of the frontal bone the cerebral atrophy, incident to old age, results in traction on the dura mater which brings about negative pressure between dura and inner table. This negative pressure is dominant in the case of the frontal bone because of the firm dural attachments on that bone coupled with the time spent in the dorsal decubitus by elderly persons. This explanation ignores the question of osmosis which would be brought into operation by negative pressure. The dura is more closely attached to the frontal bone than elsewhere in the cranium, in fact so adherent in hyperostosis that at times it cannot be loosened. Morel believes that the membrane contracts along the course of its fibers and that these are the lines of force which produce the irregular inner surface of the hyperostosis. In this Morel seems not to have encountered the sessile or flat type of hyperostosis. The existence of the flat type destroys his most ingenious theory. He also is of the opinion that the dorsal decubitus of the elderly, contributes in part to the production of the hyperostosis. An older and long held theory as to the causation of the hyperostosis, was that it was a compensatory process for filling the space produced by atrophy of the frontal lobes of the brain. Neither Greig nor Morel subscribe to this theory.

Both Greig and Morel, if they are understood correctly, consider that the hyperostosis extends from the surface of the inner table into the cranial cavity only. As far as it can be determined by roentgenography the series of cases comprising this report indicate that the dense hyperostosis progresses in both directions as has been pointed out above. Figures 3 and 4 (roentgenograms) in Morel's (loc. cit.) monograph clearly show dense bone in the diploic space.

Greig states that the hyperostosis is made up of cancellous bone with its intracranial aspect covered by a lamina of compact bone and he leaves one under the impression that he considers this cancellous bone as identical with that of the diploic space. Roentgenographically it is not identical, being much denser than the remainder of the diploe; in fact, it has the physical characteristics of compact bone. On the other hand, however, if on gross and microscopic section the hyperostotic bone is actually cancellous, then the evidence is that the bone trabeculæ contain a far greater amount of calcium than is normally the case and there is a hypercalcinosis of the diploe.

Morel insists that the hyperostosis is confined to the two halves of the vertical portion of the frontal bone (Fig. 9) and makes no mention of hyperostosis of the orbital plates of that bone (Fig. 10). Figure 4 illustrates an hyperostosis both alone and combined with involvement of the squama.

Up to quite recently on the rare occasions when this hyperostosis has been noted, it has been thought to be an incidental finding in the autopsy of aged insane persons, usually females. Greig considers the hyperostosis of no clinical moment and maintains that it is compatible with a long and active life. Certainly his material indicates that it does not affect longevity. It must be remembered, however, that his examples consisted of museum specimens, and such notes as he had on the individuals would necessarily be limited in scope; certainly too limited to permit him to consider the hyperostosis as only an involutionary change incidental to old age. He also

TABLE II.—DEGREE AND TYPE OF HYPEROSTOSIS

Hosp. No	Degree	Nodular	Sessile	Thickness in millimetersis				Other skull hyperostoses
				Inner table	Outer table	Diploe	Orbital plate	
B.H. 2788	1			Total—12			4	
B.H. 3709	1			12	1	2		
B.H. 3808	1			Total—15				Diffuse hyperostosis of calvarium
B.H. 11343	1			5	2	3		
B.H. 13163	1			7	2	1	2—	
B.H. 13823	1			Total—12				Haziness over right orbit—P.A. view
B.H. 14454	2			Total—17				
B.H. 14730	1			8	2	Trace	3	Posterior wall frontal sinus—3 mm.
B.H. 15265	2			Total—13			5	Posterior wall frontal sinus—4 mm.
B.H. 16245	2			12	2	1?	5	Posterior wall frontal sinus—6 mm.
B.H. 16376	1			Not measurable				
B.H. 17222	1			Total—15				
B.H. 17448	2			10	1+	Trace		Edentulous jaws. Sella enlarged
B.H. 18988	1			14	2	1?		Posterior wall frontal sinus—5 mm.
B.H. 19239	1			7	2	2	7	
B.H. 19791	1			6	2	2	8	
B.H. 19926	2			Total—15			Thin	Parietal hyperostosis
B.H. 20777	1			Total—9			7	Posterior wall frontal sinus—6 mm
B.H. 17626	1			Total—9				
B.H. 22295	1			10	2	3		Posterior wall frontal sinus—4 mm.
B.H. 24503	2			Total—25				Large calcification at internal occipital protuberance. Posterior wall frontal sinus—5 mm. Granular ? Atrophy
B.H. 24855	1			10	2	1	8	
B.H. 25796	2			8	1+	8		Calvarium thickened—1 cm.
B.H. 26766	2			Total—22				Posterior wall frontal sinus dense
B.H. 26864	2			Total—14				
B.H. 27303	1			Total—12				General hyperostosis of calvarium
B.H. 27450	1			10	1	2		Slight general hyperostosis
B.H. 29511	3			10	2	3		
B.H. 29520	1			6	1?	2		Posterior wall frontal sinus—4 mm.
B.H. 30163	2			Total—18				Anterior wall frontal sinus thick. Hyperostosis elsewhere
B.H. 30483	1			Total—12			4	Thin skull
B.H. 32127	1			3	1+	3		
B.H. 34347	2			Not measurable				
B.H. 35764	2			14	2	1+	4	
B.H. 35993	1			3	2	4	7	
B.H. 36667	1			Total—10				
B.H. 37551	2			15	1	3	Thin	Diffuse hyperostosis of calvarium. Destruction of sella
B.H. 37764	3			Not measurable				
B.H. 38108	2			Total—17				
B.H. 39113	2			Total—16				
B.H. 39119	1			Total—11			Dense	Posterior wall frontal sinus dense. Questionable widening
B.H. 41822	2			10	2	3		

TABLE II.—DEGREE AND TYPE OF HYPEROSTOSIS—Concluded

Hosp. No.	Degree	Nodular	Sessile	Thickness in millimeters				Other skull hyperostoses
				Inner table	Outer table	Diploe	Orbital plate	
B.H. 34180	1			14	1			Large sphenoparietal sinus
B.H. 14894	1			8	2	2		
B.H. 16043	3			Total—43			5	
B.H. 17338	1			8	2	3		General hyperostosis. Bridged sella
B.H. 18072	3			11	2	Trace	4	Posterior wall frontal sinus—5 mm.
B.H. 18091	3			Total—23				
B.H. 18884	1?			6	1	.3		
B.H. 19456	1			9	1	Trace		Posterior wall frontal sinus—6 mm.
B.H. 21582	2			17	1	2		
B.H. 24172	1?			Not measurable				General bone atrophy. Acromegalic type
B.H. 41058	2			14	2	3		
B.H. 42606	1			Not measurable				Calvarium thin
B.H. 42710.	'24 1 '34 2			13 16	3	Trace		
O.P.D. C3194	3			Total—19				
O.P.D. C12741	1			Total—15			4	Posterior wall frontal sinus—7 mm.
O.P.D. C50756	3			Total—46			10	General hyperostosis. Posterior wall frontal sinus thick. Parietal—20 mm.
O.P.D. B74454	2			Total—15				Posterior wall frontal sinus thick
M.S.-Pvt.	1			5	1	3		
T.S.-Pvt.	1			8	2	4		
B.S.-Pvt.	1			Total—14			5	Posterior wall frontal sinus—7 mm.
H.S.-Pvt.	2	Mixed		7	3	2		
D.S.-Pvt.	1			6	2	1		
J.S.-Pvt.	1				3			Hyperostotic area—12 mm. Destruction of sella
R.M.-Pvt.	1?			Total—12				Thin skull
E.H.-Pvt.	2			5	1	3		Large bilateral sphenoidal sinus
V.D.-Pvt.	2			Total—13			6	
M.B.-Pvt.	2			9	2	3		
L.M.-Pvt.	1			4	1+	3		
R.H.-Pvt.	2			Total—18				Ossification of falx
M.C.-Pvt.	2			12	2	4		

appears to ignore the fact that 28 of his 32 patients, or 87.5 per cent, were women. All of the cases of Stewart, Morel, and Naito, were insane though they were all of an advanced age. The cases of Van Bogaert and Schiff and Trelles of less advanced years were of such severity as practically to disable the patients. It is apparent that in its full development this syndrome is associated with psychosis. Seventy of the 72 cases comprising this study were all of a degree of morbidity calling for medical and, in 55 cases, hospital care. The study of their clinical histories is convincing proof of their invalidism. The average age, 44 years, the degree of hyperostosis, and the intensity of the accompanying symptoms were less than those of Morel and Stewart. The study of the 70 cases suggests that there is progression of the disease, which may reach the extreme seen in the material Stewart and Morel have reported in the literature.

TABLE III

Hosp. No.	Age Sex	Race	Pregnancies	Entered hospital for	Complications	Serology	Metabolic disease	Degree	Neurologic
B.H. 2788	35 F	W	none	Occipital pain. Sciatic neuritis	Lumbar arthritis	+	Obese	1	Fatigue
B.H. 3709	54 F	W	1	Diabetes	Osteo-arthropathy Hypertension	–		1	Psychasthenia
B.H. 3808	38 F	W	4	Frontal headaches	Tumor of brain suspect	–	Obese	1	
B.H. 11343	34 F	W		Edema of legs. Depression. Multiplicity of complaints	Hyperthyroid. Hypochondriasis	–	Obese	1	
B.H. 13163	32 F	W	1	Sudden loss of vision, rt. eye. Lt. eye blind	Hypothyroid. Transphenoidal op. neg.	–	Obese	1	Weakness. Cranial nerves negative*
B.H. 13823	25 F	W	2	Diplopia 2 yrs. Speech difficulty	Thyroidectomy	–		1	Mentally dull
B.H. 14454	53 F	W	2	Pain lt. eye and face. Swelling of lids	Meningitis. Suppurative sinusitis	–	Obese Diabetes	2	†
B.H. 14730	22 F	W	none	Headache	Appendectomy Tonsillectomy Nephropexy	–		1	
B.H. 15265	35 F	W	none	Headache. Convulsion	Hydrocephalus	–	Obese	2	Skull defect
B.H. 16245	59 F	W		Aphasia, 3 yrs. Pain over lt. eye. Headaches	Hypertension	–		2	Vague mentally. Speech difficulty
B.H. 16376	65 F	W	5		Ca.uterus	–		1	
B.H. 17222	48 F	W		Headache. Failing vision. Deafness	Bilateral choked discs	–		1	Certified Fibroblastoma 8th nerve
B.H. 17748	56 F	W	4	Headache. Failing vision. Mentally dull	Exploratory craniotomy negative	–	Obese	2	Ringing in ears. Mentally dull
B.H. 18988	52 F	W	none	Headache. Arthritis. Deafness	Hypochondriasis. Hypertension	–		1	Nervous. Paralysis 7th nerve
B.H. 19239	18 F	W		Headache, occipital. Neurosis		–		1	Fatigue. Emotional
B.H. 19791	26 F	Col.	none	Headache, occipital. Failing vision	Osteosarcoma skull shoulder. (?)	+		1	Weakness. Tenseness
B.H. 19926	75 F	W	3	Headache, frontal. Diplopia. Vertigo. Nausea		–		2	6th nerve weakness
B.H. 20777	35 F	W	none	Jacksonian epilepsy 16 years		–		1	
B.H. 17626	57 F	W		Trigeminal neuralgia 5th. Dizziness. Neurosis. Failing vision. Shortness of breath	Gasserian ganglion. Op.	–		1	Rt. facial weakness. Ringing and buzzing in ears. Dizziness
B.H. 22295	28 F	Col.	3	Headache. Pain behind left eye		–		1	Dim vision. Hysteria. Spasmodic movements of face and head
B.H. 24503	46 F	W	none	Headache. Dim vision lt. eye. Arthritis	Chr. cystitis mastitis. Deaf lt. 10 yrs.	–		2	Irritability. Weakness
B.H. 24855	24 F	W	1	Hypochondriasis. Headache, frontal, dull	Head injury accident	–		1	Nervous. Dizziness. Ringing in ears
B.H. 25796	78 F	W		Traumatic case	Fracture of clavicle	–		2	
B.H. 26766	44 F	W		Traumatic case		–		2	Hysteria
B.H. 26864	24 F	W		Epilepsy, grand and petit, many years		–		2	
B.H. 27303	44 F	W	3	Fatigability	Hyperthyroidism	–	Obese	1	

TABLE III.—Continued

Hosp. No.	Age Sex	Race	Pregnancies	Entered hospital for	Complications	Serology	Metabolic disease	Degree	Neurologic
B.H. 27450	52 F	Col.	1	Diabetes			Obese	1	
B.H. 29511	44 F	Col.	21	Headache, frontal. Pansinusitis	Osteomyelitis frontal bone?	–		2	
B.H. 29520	23 F	W	none	Headache, severe, 6 mos. Bilateral choked discs	Op. chr. left mastoiditis	–		1	
B.H. 30163	51 F	W	6	Obesity. Allergy	Dermatitis. Hypertension	–	Obese	2	
B.H. 32127	62 F	W	2	Headache, occipital, frequent with vomiting	Arteriosclerosis Chondystrophia fetalis	–	Obese	1	Rt. 7th paralysis Mentally dull
B.H. 30483	43 F	W		Headache, occipital and parietal, severe. Unsteady gait		–		1	Progressive weakness‡
B.H. 34347	40 F	W	4	Psychoneurosis. Failing vision 3 yrs.		–	Obese	2	Nervous
B.H. 35764	35 F	W		Headache. Fatigue. Brain tumor suspect	Sinusitis 4 years	–		2	Dizziness. Blurring left eye. "Tickling" of tongue
B.H. 35993	48 F	W		Migraine. Severe headache 25 years. Allergy	Sphenoidal sinusitis	–		1	Fatigue. Talkative. Querulous. Cranial nerves negative
B.H. 36667	42 F	W		Epileptic attack 18 mos. previously		–	Obese	1	Nervousness
B.H. 37551	64 F	W		Headache, frontal, 8 mos.	Arteriosclerosis	–	Obese	2	Nervousness
B.H. 37764	59 F	W	4	Arthritis deformans	Chr. sinusitis	–	Obese	3	
B.H. 38108	60 F	W		Arteriosclerosis. Myopia. Sl. deaf. Headache	Sinus op. Hypertension	–	Obese	2	§
B.H. 39113	56 F	W		Headaches, 2 yrs. Nervousness	Craniotomy. Fibroblastoma 8th nerve	–		2	Nervous. Eyes prominent. Fibroblastoma 8th nerve
B.H. 41822	54 F	W	2	Headache. Petit mal at 52	Consulated EENT.	–		2	
B.H. 39119	48 F	W	4	Dim vision, 3 yrs. Arteriosclerosis		–		1	
B.H. 34180	59 F	W	4	Staggering gait. Poor memory. Falling to rt. and left	Possible cerebral arteriosclerosis	–	Obese	1	Mentally dull. Unable to write at times
B.H. 14894	65 F	W	2	Neuralgia 5th nerve. Dim vision	Mastoid op.	–		1	Tinnitus. Dim vision. Impaired hearing
B.H. 16043	28 F	W	1	Tumor of brain suspect, uncertified. Headache, occipital, 3 mos.	Accident 3 yrs. ago, no symptoms until 1 yr. ago	–	Obese	3	Numbness lt. arm. Tingling and crawling sensation of scalp and lt. leg
B.H. 17338	31 F	Col.		Neurosis. Dragging lt. leg	Myoma uterus	–		1	Nervous. Irritable
B.H. 18072	35 F	Col.	5	Tbc. 4th dorsal vertebra Paraplegia	Chr. cystitis	–	Obese	3	Numbness, weakness. Bilateral Babinski
B.H. 18091	40 F	W	9	Headache, occipital and frontal with nausea and vomiting. Dizziness 20 years. Arthritis. Dyspituitarism	Osteoarthritis Chr. cholecystitis	–	Obese	3	Dizziness
B.H. 18884	54 M	Col.		Steady headache 5 yrs. Vertigo. Nervousness	Osteoma left femur. Chr. sphenoiditis, operation	–		1	Nervousness. Fatigue
B.H. 19456	72 F	W	2	Headache. Hemiplegia. Vertigo. Vomiting		–	Obese	1	

TABLE III.—Concluded

Hosp. No.	Age Sex	Race	Pregnancies	Entered hospital for	Complications	Serology	Metabolic disease	Degree	Neurologic
B.H. 21582	55 F	Col.	none	Headache, 5 yrs. Failing memory. Nervous. "Paralysis"	Meningeal fibroblastoma	–		2	Failing memory. Nervousness
B.H. 24172	57 F	W	8	Headache, frontal and occipital. Bilateral hemianopsia	Craniotomy, exploratory	–	Obese	1	Failing vision**
B.H. 41058	32 F	W	2	Headache, frontal, 2 yrs. Nausea and vomiting. Failing vision. Tumor of brain suspect		–		2	7th ? nerve weakness
B.H. 42606	31 F	W	4	Headache, severe. Migraine. Hemorrhage left eye. Diabetes		–		1	
B.H. 42710	52 F	W		Headache, severe. Hypertension. Obesity. Arteriosclerosis	Pituitary tumor ?	–	Obese	'24 1 '34 2	
OPD. C3194	29 F	W	1	Headache, throbbing. Migraine. Myopia, rt.		–		3	Nervous. Poor memory
OPD. C12741	25 F	W		Headache. Dizziness, 10 yrs. Tendency to fall		–	Obese	1	Fatigue. Dizziness
OPD. C50756	46 F	Col.		Headache, frontal, since childhood		–	Obese	3	Dizziness. Worry
OPD. B74454	48 F	W		Headache	Chronic sinusitis	–		2	
M.S.-Pvt.	38 F	W		History unavailable				1	
T.S.-Pvt.	32 F	W		History unavailable				1	
B.S.-Pvt.	40 F	W		History unavailable				1	
H.S.-Pvt.	56 F	Col.		History unavailable				2	
D.S.-Pvt.	26 F	W		History unavailable				1	
J.S.-Pvt.	42 F	W		History unavailable				1	
R.M.-Pvt.	14 M	W		History unavailable				1?	
E.H.-Pvt.	37 F	W		History unavailable				2	
V.D.-Pvt.	52 F	W		History unavailable				2	
M.B.-Pvt.	32 F	W		History unavailable				2	
L.M.-Pvt.	54 F	W		History unavailable				1	
R.H.-Pvt.	41 F	W	2	Fatigue, depressed		–	Obese	2	Fatigue, depressed
M.C.-Pvt.	50 F	W		Recurrent headaches				2	

*Exploratory. Craniotomy
†Autopsy. Acute meningitis
‡Autopsy report. Medulloblastoma, rt. cerebellar angle
§Autopsy. Meningeal hemorrhage
**Questionable solid tumor of hypothalamic region

Morel's living case was 81 years of age and had been confined to the asylum for 30 years. The roentgenograms of the skull show a pronounced degree of internal hyperostosis. It can be taken as an example of this disorder in its complete form. Van Bogaert's case was a female, aged 66 years, with progressive mental deterioration and obesity. There is also

the interesting fact that her blindness was attributable to disturbance in the visual center and presumptive pressure on the optic nerve in the orbital foramen. This latter finding is of the first importance. The case of Schiff and Trelles was a male, aged 60 years. Following an accident with concussion of the brain the patient had headache, convulsions, and personality change. There was disturbance of gait and equilibrium and a negative Wassermann. Roentgenography revealed a typical internal frontal hyperostosis. Schiff and Trelles summarized the findings in their patient as follows:

"A psychic syndrome characterized by
a. Intellectual slowness, depression, and anxiety,
b. Disturbance of temperament and of character,
c. Protective neurosis.

Neurological syndrome—
a. Continuous headache with paroxysmal exacerbations,
b. Difficulty in gait and equilibrium,
c. Obesity of the hypophyseal genital type, extreme.

Changes in the serum balance—
a. Hypercalcæmia.
b. Deficiency in the hydrogen-ion concentrations in the direction of an acidosis without change in the alkaline reserve."

In the 7 autopsy reports, 3 by Stewart and 4 by Morel, the patients were generally obese and there was frequently a fatty infiltration of the skeletal muscles. Arterial calcification and arthritis appear to be no more frequent than would be the case in persons of like age. Except for the hyperostosis of the skull there is no mention of any particular bone change. However, bone changes have not been sought for systematically either at autopsy or, what would be a surer method, roentgenographically. In Stewart's cases there was a disappearance of the cellular elements in the pituitary with replacement by fibrous tissue. He considered the changes as of little consequence and as being approximately those to be anticipated in old people. The dura mater is reported as being intimately attached to the hyperostotic zones by Stewart, Morel, and Greig, and all signs of inflammation of this membrane and the underlying bone, past or present, are lacking. The surface of the bone is smooth. Both Morel and Greig write that there is no hyperostosis of the base of the skull. To digress at this point—It must be pointed out that hyperostosis in that location might easily escape observation at autopsy, whereas it could be readily discovered roentgenographically.

TABLE IV.—INCIDENCE BY DECADES

1	2	3	4	5	6	7	8
0	2	11	15	16	20	5	3

In 4 of his cases, Morel made serial sections of the third ventricle from a point just in front of the anterior commissure to the mamillary bodies. There were cellular lesions in the wall of the third ventricle which were sharp. They consisted of an excess of pigment and fat in the cells producing a granular appearance almost to the point of cellular disappearance. His conclusion is that there is present in hyperostosis frontalis interna a lesion in the wall of the third ventricle and that the cause of the lesion is also the cause of the syndrome. It is significant also that Case B.H.24172 had a questionable solid tumor of the hypothalamic region. Stewart's pathological material excludes the pituitary as having any part in this disorder with some question as to its posterior lobe.

Since in this series of cases, 97.2 per cent are females and the average sex incidence of the cases reported by Naito, Stewart, Greig, Morel, Van Bogaert, Schiff, and Trelles is 82 per cent females, it is clear that the disorder is one so dominantly found in the female that differential diagnosis does not have to be concerned with those disorders which affect the sexes equally. This at once rules out any possibility of its being traceable to a deficiency disease. It likewise removes it from the class of such endocrine disturbances as have an equal or even nearly equal incidence in the two sexes. The evidence all points to the disease being one referable to some structure peculiar to the female. With the tabulation of the pregnancies given here, it is difficult to see how this disorder can be attributed to the ovary.

It is self-evident that there is a mechanism common to both sexes for the control of calcium metabolism. Because of the functions of the female, which are related to calcium metabolism, it seems almost inescapable that the sex has a special mechanism for its control. Since hyperostosis frontalis interna occurs almost exclusively in women, it is proposed that there is a special structure present in the female which governs the calcium metabolism essential for menstruation, gestation, and lactation. These three functions require the assimilation and disposal of an enormous amount of calcium and the requirements are intermittent. Now if such a theoretical mechanism should not undergo involution in step with that of the sex organs of the female of known function there might result an aberration in calcium metabolism. This appears to take place in hyperostosis frontalis interna, the deviation from normal being the retention of calcium which should be eliminated. The involution of such a calcium control mechanism should be greater with advance in years. In this condition, however, involution is not in equilibrium with that of ovary, uterus, and breast; it may be that it is precocious, and hyperostosis frontalis interna a manifestation of premature old age. There is a strong temptation to draw an analogy between hyperostosis frontalis interna and chronic cystic mastitis. The material of this study, however, indicates that it is by no means confined to elderly persons but merely that it is more likely to be found in its extreme form in old age. However this theory may be, it is certain that there is a disorder of calcium metabolism found in women and, despite clinical reports which are few in number, only questionably occurring in the male. Morel's pathological findings are very suggestive in implicating the third ventricle as the locus of this theoretical mechanism.

Little is to be said as to prognosis until this syndrome has received much more study than it has, and its true nature is better understood. Until then the prognosis, certainly in a proportion of cases, is progressive nervous and mental deterioration and a terminal insanity in the extreme cases and long continued morbidity in those less pronounced. Perhaps therapeutic indications may modify the prognosis.

It is fortunate, indeed, that in this condition there are certain clear cut therapeutic indications. Before considering them, thought is to be given certain diagnostic steps which should be taken in every suspected case. These are a painstaking analysis of the subjective history and of the symptoms, especially those of the cranial nerves. Study of the calcium-phosphorus metabolism and the acid base equilibrium of the blood serum should be done. The case of Schiff and Trelles emphasizes the necessity for this. Roentgenologically the examination should be more comprehensive than has been the case. This undoubtedly applies to the material in this study. There should be as a minimum a stereoscopic examination in the lateral projections from both sides of the skull, a stereoscopic examination in the postero-anterior projection, and an examination of the optic foramina; the latter is mandatory in cases such as that of Van Bogaert, as it is indeed in all cases. Until encephalography has been proved a useless procedure it should be carried out as a routine measure when there is a suspicion of any form of intracranial hyperostosis.

If metabolic studies reveal a faulty calcium-phosphorus balance or a disturbance of the acid base equilibrium then dietary experiments should be tried for the purpose of restoring metabolic balance. The use of parathyroid hormone appears to be distinctly worth a trial, as does a rachitic diet, to counteract excessive calcium deposit. A digression is in order at this point. Negative findings in a single chemical examination of the blood for calcium content cannot be taken as indicating a normal condition. Detecting a slight hypercalcemia is difficult and success in finding it must be, so to speak, accurately timed with the height of the changes which produces the hypercalcemia. Now, if hyperostosis frontalis interna is the result of hypercalcemia, let it be remembered that this disorder is one of slow progression and there might be periods of arrest and possibly of remission; further, at no time would there be an extreme hypercalcemia.

If there are signs of increased intracranial pressure as a result of hyperostosis, on theoretical grounds, surgical intervention promises much. Indeed, exploratory operation of the frontal area is indicated in the absence of increased intracranial pressure if the symptoms accompanying hyperostosis frontalis interna are of a severity to warrant major steps. Unquestionably, Jacksonian episodes (not infrequent) in conjunction with a frontal hyperostosis are an operative indication. Compression of the optic nerves, and this should be ascertainable at all times by roentgenographic methods, calls for surgical interference along the optic groove in those cases in which there is a hyperostosis of the orbital plate of the frontal bone. Massive projections of bone extending into the cranial cavity such as case O.P.D. C50756 (see Fig. 2) certainly seems to call for removal as clearly as would a depressed fracture encroaching to this degree on the substance of the brain. Atrophy of the cerebral cortex beneath the nodulations of hyperostosis frontalis interna is reported. Because this atrophy is found in a "silent area," it does not follow that such nodulations are harmless. With the little knowledge there is regarding these "silent areas" it is unjustifiable not to deal with them just as would be done with an hyperostosis occurring in a region of the brain where focal symptoms result.

There are certain points that have been discovered at autopsy in this condition which are surgically suggestive. The first of these is that the groove for the longitudinal sinus does not share in the bony thickening. The other is that the outer layer of the dura is intimately attached to the bone, and this point is emphasized by all of the authors who have written on the subject. From their descriptions, this attachment seems to be so firm that it would be impossible to elevate the bone without rupture of the dura.

It has been mentioned that, if the optic nerves are jeopardized by local pressure, this constitutes a surgical indication for intervention. Though it has not been mentioned by others and was not found in the clinical analysis in the cases of this report, it is possible that the olfactory nerve might also become so strangulated as to give rise to important symptoms. The fact that this nerve penetrates a bone pre-formed in cartilage has been noted above. It also should be remembered that its exit from the cranium is near the midline, which region, at least in the case of the vertical portion of the frontal bone, is free from the hyperostosis, and the cribriform plate might, because of its location, likewise escape the hyperostosis.

CONCLUSIONS

In conclusion it can be said that hyperostosis frontalis interna is by no means the medical curiosity which the percentages here given appear to make it. There is a total of 65 cases described in the literature, all but 3 being either autopsy reports or composed of museum specimens. To this number 72 living examples of the condition have been added. In spite of the different degrees or types of the disorder, the cases have an astonishing similarity to each other and there is variation only in the intensity of the symptoms. Against the severity of the syndrome, one may say tragedy in its full development, stands the fact that there are many rational therapeutic measures which may alleviate or possibly arrest the disorder. It is a fact that the picture of the syndrome in its complete form has been published by several writers; description of its less advanced development is something that is new. Two hypotheses regarding hyperostosis frontalis interna have been offered: first, that there is a special mechanism for the control of calcium metabolism, existing only in the female; and second, that the disorder of such a mechanism is the cause of the syndrome accompanying hyperostosis frontalis interna. There is presented a field which should be a fruitful one for investigation of those fundamentals which underlie the physiology and chemistry of calcium and fat metabolism, and possibly a hitherto unknown structure with an internal secretion. The disease will be found with far greater frequency if it be sought for. It is possible that investigation of this disorder may throw much light on neuropsychiatric pathology. There is a question as to whether or not the unknown causative factor which

produces the syndrome does not also give rise to the neuropsychiatric symptoms as well as the hyperostosis. Hyperostosis frontalis interna as a name for this syndrome suffers from the drawback inherent in using a single feature of a disorder to designate the whole. It is possible that the hyperostosis, though the surest sign, is the least important manifestation of the disease.

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A LYMPHATIC CONNECTION BETWEEN THE GALL BLADDER AND LIVER[1]

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FOR many years since the investigations of Sappey (1885) and Sudler (1901) it has been rather generally accepted that a lymphatic connection between the gall bladder and liver exists. Sudler, using for the most part dogs and pigs, injected carmine gelatin into the portal vein at a pressure of 80 millimeters of mercury for 15 minutes and states that by this means he could inject the lymphatics of the liver and in turn the larger lymphatics over the gall bladder and finally those in the subserous coat of the gall bladder.

In 1918, one of us (E.A.G.) described constant inflammatory changes occurring in the liver associated with cholecystitis. These consisted of polymorphonuclear or round cell infiltrations, according to the acuteness of the infection, in the interlobular, or periportal, sheaths. In the more acute infections the parenchyma at the peripheries of the lobules showed infiltration with an associated edema, slight necrosis, and fat infiltration.

Based largely upon the early work of Sudler which demonstrated existence of a lymphatic connection between the liver and gall bladder, one of us (E.A.G.) and co-workers (Priest and Peterman) in 1921, stressed for the first time the probable great importance of the lymphatics as one of the possible routes of infection between the gall bladder and liver regardless of which organ might be primarily affected in a given case. Previous to this time the pathogenesis of infections of the gall bladder and bile tracts was based on four assumed possibilities: (1) descending infection from the liver by bacteria carried down in the bile, (2) ascending infections from the duodenum up the lumen of the common bile duct, (3) hematogenous infections of the gall bladder and ducts, and (4) a spreading infection through the wall of the gall bladder from an inflamed contiguous organ.

That the lymphatic route is an important one has been accepted by many writers. However, in 1927, Winkenwerder working at Johns Hopkins on the lymphatics of the gall bladder of the cat was unable to demonstrate a connection between the liver and gall bladder. By the direct injection of India ink into visible lymphatics of the subserous plexus of the gall bladder, followed by formalin fixation of the specimen, clearing by the Spalteholz method, and subsequent study of the gall bladder wall under the dissecting binocular microscope, Winkenwerder demonstrated nicely the three lymphatic plexuses in the wall of the cat's gall bladder and the anastomoses of each with the others. However, he states that a careful search failed to reveal any intercommunication between the lymphatic plexuses of the gall bladder with the lymphatic vessels of the adjacent liver tissue.

These observations naturally gave rise to serious doubt as to the actual existence of such a lymphatic connection and in turn challenged the validity of any theory holding the lymphatics responsible in certain cases for hepatitis secondary to a cholecystitis, and vice versa. Hence, it seemed to us important to reopen the question.

METHOD

The cat was chosen as the experimental animal because of its rather uniform size, the ease with which it is obtained, and, lastly, because it was the only species of animal which Winkenwerder used.

Of the several possible modes of attacking the problem, the one which seemed to us to give promise of offering the most conclusive results was that of direct injection of a dye into visible lymphatics of the gall-bladder wall in the hope that the injected material would appear in the lymphatic spaces of the adjacent liver tissue.

It is a well established fact that in order to obtain satisfactory retrograde injections of the gall-bladder lymphatics, the valves present in

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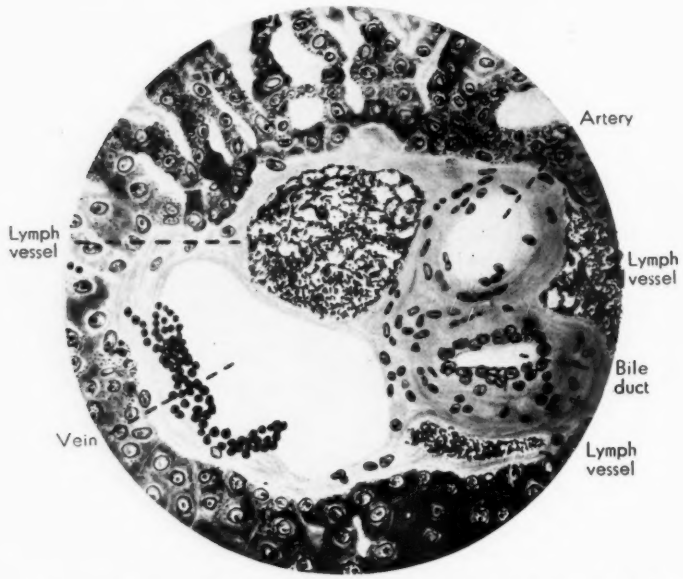

Fig. 1. Hematoxylin and eosin preparation. The light blue material is the dye which was injected into the lymphatics of the gall bladder, and it is seen here very clearly to be present in periportal lymphatic vessels in the liver. The bile duct, the artery, and the interlobular vein are clearly distinguishable. The only possible source of transport of the dye into the liver, under the conditions of the experiment, is therefore anastomosing lymph channels between the two organs.

some of the larger ones must first be rendered incompetent. This, therefore, was accomplished by utilizing the method described by Lee which consists of ligating under intratracheal anesthesia the thoracic duct in the chest as a preliminary step, the result being a generalized dilatation of the abdominal lymphatics which causes the valves whenever present to become incompetent. It might be added that unless the animal is fed cream 3 to 4 hours before operation, the greatest difficulty is encountered in visualizing the duct.

After waiting 2 to 4 days the abdomen was opened through an upper right rectus incision and the expected dilatation was found. The subserous lymphatics of the gall-bladder wall were usually clearly seen and it was interesting to note that additional dilatation of these can be obtained for a short time by placing a clamp across the cystic duct and adjacent tissues, thus completely blocking the several main lymphatic trunks of the gall bladder.

Beale's Prussian blue was the dye selected as the injection material and a No. 28 gauge hypodermic needle and small syringe were used. The needle was carefully introduced into the largest available subserous lymphatic and usually about 1 cubic centimeter of the dye was injected over a period of from one half to one minute. This gave a very clear picture of the lymphatic network of the region injected. Immediately either the entire liver or, as was more often the case, the gall bladder and adjacent liver tissue was removed and placed in 10 per cent formalin for fixing, after which routine paraffin sections were made for microscopic study. In some cases sections were taken to show both gall bladder and liver; in others only the liver tissue was included. Two adjacent sections were always stained; one with eosin only so that any of the blue dye present might be readily located, the other with hematoxylin and eosin, that the various structures in the section might be identified in relation to the dye injected.

CONCLUSIONS

The dye injected into visible lymphatics in the subserous layer of the gall-bladder wall

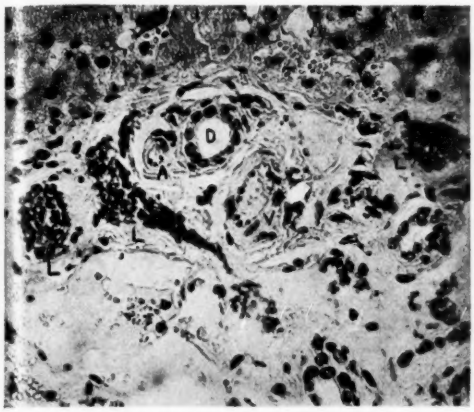

Fig. 2. A periportal area containing in a group *L* three lymphatic vessels filled with the injected dye, *A* an artery, *V* a vein, and *D* a bile duct.

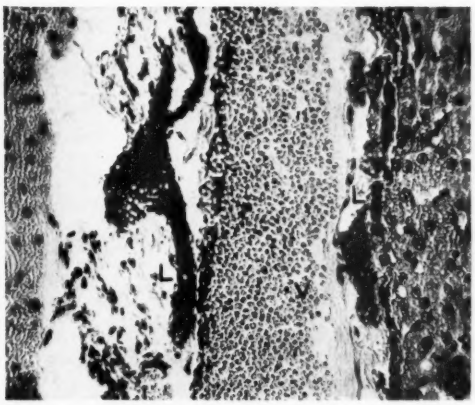

Fig. 3. This shows *V* a longitudinally cut blood vessel and *L* two perivascular lymphatic vessels containing the injected dye. These structures are surrounded by liver parenchyma.

was found repeatedly to have passed into the adjacent liver tissue and there to be located in perivascular and periductal endothelial lined vessels in the portal spaces. As will be noted in the illustrations the usual picture shows an epithelium lined bile duct, an artery and vein containing red blood cells, and one or more endothelium lined vessels with the dye present in a group and surrounded by liver cells.

This evidence seems, therefore, definitely to substantiate the earlier work of Sudler in demonstrating the existence of an intimate lymphatic anastomosis between the gall bladder and the liver. These particular experiments of ours have shown the transportation of the dye only into the portion of liver immediately adjacent to the gall bladder. But from what is already known about the distribution of the lymph in the liver, from the work of Mall, there is good reason to suppose that the dye in time would have been found elsewhere, at least in other parts of the right lobe, if the experimental method had permitted finding it. Since, however, only very small amounts of dye were used, it was difficult to recognize its presence at more remote parts of the liver where it would occur in only very slight concentration. At any rate the anatomical evidence of the hepatitis which occurs in association with cholecystitis is most marked in the right lobe of the liver and particularly in that part of it which is immediately adjacent to the gall bladder. In other words, the agreement between the distribution of the dye transported to the liver by way of the lymphatics and the distribution of the histological evidences of inflammation seem to lend additional support to the idea that, at least in some cases, there is a lymphatic transport of infection between gall bladder and liver.

The fact that, as Noble has recently emphasized, at postmortem examination there is frequently found an infiltration of the periportal spaces with lymphocytes and polymorphonuclear leucocytes, regardless of any demonstrable disease of the gall bladder, has little to do with the point under discussion in this paper. We have never proposed that the gall bladder is the only source of a periportal lymphangitis in the liver.

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CLINICAL SURGERY

FROM THE UROLOGIC SERVICE, LEWISHAM HOSPITAL, SYDNEY

RECONSTRUCTION OF THE FEMALE URETHRA

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FIVE patients afflicted with complete destruction of the urethra in association with vesicovaginal fistula have been encountered by the author in the past 10 years. Twice the lesion was due to sloughing following childbirth; and on the other 3 occasions was the outcome of the surgical treatment of carcinoma of the urethra by resection, diathermy or radium used either alone or in various combinations.

Since in the circumstances for which the operation is to be undertaken, the bladder sphincter and posterior wall of the urethra have been more or less completely destroyed, for this reason it will be necessary not only to fashion a new urethra but also to provide it with an efficient cut-off muscle.

As no recorded type of operation for this comparatively rare lesion appears to have inspired any kind of enthusiasm, or to have been hailed with even the mildest degree of satisfaction, and especially as reports still continue to appear in the literature of results, too often only partially successful, which have followed attempts at the surgical repair of this condition (cf. McGlinn and George Gray Ward), the author has been prompted to place on record again an operation which he has employed with success in the treatment of the 5 patients here mentioned. The results obtained, from the patients' point of view, appear to leave little room for improvement. All have complete bladder control.

In the case of the first three of these patients a brief description of the operation was presented at the first annual meeting of the Royal Australasian College of Surgeons held at Canberra in March, 1928, and was published in *The Journal of the College of Surgeons of Australasia*, March, 1929. Since that publication some small technical modifications have been made. The operation has now been redrawn and is described herewith in further detail.

OPERATIVE TECHNIQUE

Some tags or bands of tissue are liable to be present in the region of the urethra, especially in post-obstetric cases. These should be trimmed off level with the vaginal mucosa and allowed to heal before the plastic operation is undertaken.

Briefly, the operation consists of making a U-shaped incision surrounding the vesicovaginal orifice, the open end of the "U" terminating at the original site of the external orifice of the urethra (Fig. 1). The incision is deepened for about 3 millimeters (one-eighth of an inch) and the vaginal wall beyond the line of incision is undermined all round to form lateral flaps. The portion of the vagina embraced by the U-shaped incision is not further disturbed, except by the sutures employed to bring its edges together in the midline to reform the urethral tube (Fig. 1, inserts a, b, and c). A new sphincter is then fashioned from the muscles of the bladder base as will be described below (Fig. 2, insert a) and the lateral flaps are sewed together over-all, the restoration of the urethra being thus completed (Fig. 2, insert b). Actually the neighborhood of the fistula is covered by three or four superimposed layers, whereas in the lower part of the new urethra only two layers are formed. A suprapubic cystotomy concludes the operation. Urethral drainage is not practiced.

The operation is very simple and makes use of principles well known in the plastic surgery of the male urethra. The absence of tension leaves little room for failure when reasonable precautions are taken.

It will, perhaps, not be amiss if some features of the operative technique be described in further detail.

After the U-shaped incision has been outlined, the lateral dissection must be carried fairly deeply and widely in the region of the base, so as to allow a good exposure of the bladder muscle in the

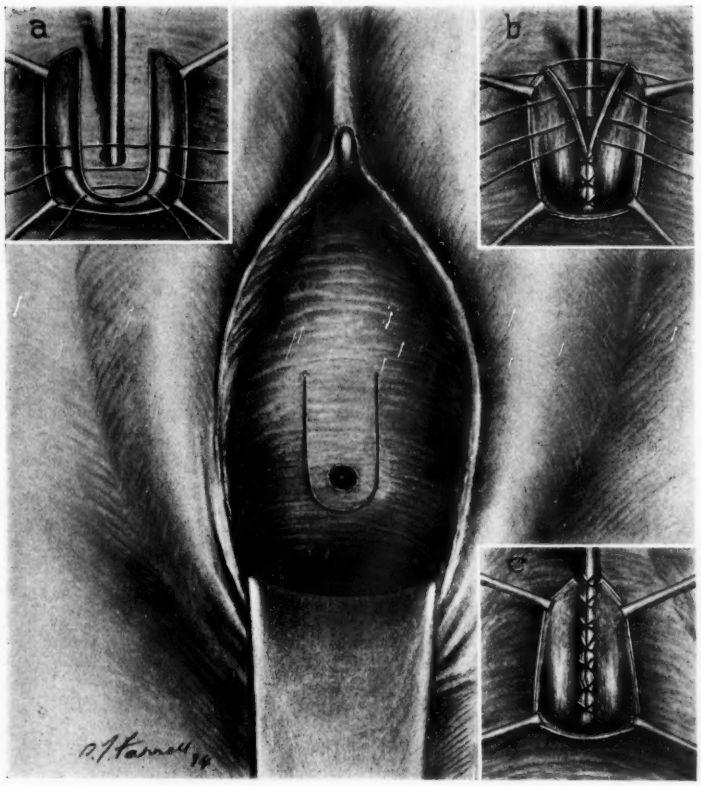

Fig. 1. Showing U-shaped incision around orifice of vesicovaginal fistula and site of urethra. a, Showing Young's seminal vesicle tractor in the bladder and first three sutures in position, but not tied. In practice each suture is tied as it is inserted. b, First three urethral sutures tied; the remainder inserted but not tied. c, All urethral sutures tied; urethral tube reformed.

neighborhood of the fistula. Toward the free ends of the U, however, there is no underlying bladder muscle and the dissection in this situation should be much more superficial (Fig. 2). If the dissection be carried too deeply, large venous plexuses may be encountered, the bleeding from which may be difficult to control. This mistake was actually made in the first 3 cases in an endeavor to obtain more tissue than was absolutely necessary. In the last 2 patients, care was taken to dissect only deeply enough in this situation to allow easy approximation of the cut edges.

Young's seminal vesicle tractor was employed in the last 2 cases and is a great improvement on the de Pezzer catheter which was employed in the first three. An instrument of this type is invaluable in delineating the bladder neck and so in indicating the exact situation for the insertion of the sutures for the sphincter reformation.

In the process of reforming the sphincter, if a sufficiently firm grip of the tractor is not afforded, when the two sutures illustrated have been tied, another suture should be placed more widely at a level midway between these two sutures. This additional sphincter suture was employed in each of the last 2 cases, and could probably be employed with advantage in all. The tractor is kept in position until the completion of the plastic operation.

Chromicized gut No. 0 is used for the first or innermost layer of sutures, No. 3 plain catgut for the sphincter sutures, and silkworm-gut for the final vaginal sutures. As large a bite of the tissues as is reasonably possible is included in each suture.

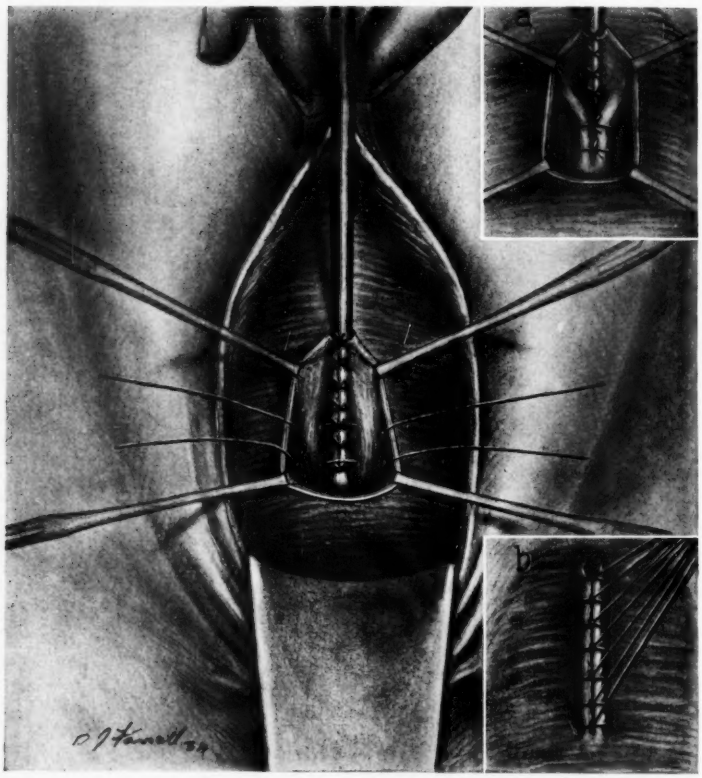

Fig. 2. Showing the two sutures in position for reformation of the sphincter. a, Sphincter sutures tied. b, Completed operation; individual sutures uniting the vaginal mucosa in the midline.

Interrupted sutures of silkworm-gut for the outer layer were used only in the last two patients and *per primam* union resulted. Equally good results were previously obtained when continuous catgut sutures were employed, but it is believed that in a larger number of cases, a slightly higher degree of certainty would be obtainable with the interrupted silkworm-gut sutures. These may be left in position until the twelfth or fourteenth day, when the suprapubic drainage is dispensed with. Rapid closure of the suprapubic wound ensued in all cases.

CONCLUSIONS

A perusal of the literature would lead one to believe that the necessity for an operation of the type described arises more commonly in America than in England or Australia. Recorded cases are, however, by no means always an accurate guide to local conditions. Be this as it may, the author's operation is presented to his American colleagues in the fervent hope that, should the occasion arise, the operation will yield results in their hands at least as satisfactory as it has in his.

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PULMONARY EMBOLISM FOLLOWING TRAUMA

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NUMEROUS papers have been written on traumatic thrombosis without embolism but, of the almost countless papers on pulmonary embolism, only a few are devoted to the type following injury. These are mostly isolated case reports. The only large reviews I have found are those of Bruns (1886), Lotheissen (1902), and Daus (1913).

In 1927, I reported 23 cases of pulmonary embolism following injury and found 119 cases in the literature. Since that time a considerable number of instances of post-traumatic embolism have been reported, many only as incidental to the whole problem of embolism of the lung and not in sufficient detail to permit of tabulation. Lister (1927) reported 12 cases following fractures in a series of 281 pulmonary embolisms. Of the 12, 9 followed fracture of the femur, an incidence of 11 per cent in 80 fractured femurs. Henderson (1927) reported 5 cases in a series of 313 embolisms, 3 of them following reduction of fractures of long bones. Hoering (1928) reviewed 3,248 autopsies, finding 131 instances of pulmonary embolism, 10 of which were post-traumatic. Of the 10 cases, 4 followed fracture of the femur. Martini (1928) reported 90 cases of pulmonary embolism from a series of 3,193 autopsies. Five of the embolisms followed fracture. In a series of 113 cases of embolism reported by Miller and Rogers (1929), 7 followed fractures but necropsies were done in only 4 of these traumatic deaths. Killian (1930) reported 102 instances of embolism, tabulating 35 of these. In his table 5 instances of postfracture embolism are cited. Orator and Straaten (1930) found 3 of post-traumatic origin among 17 fatal embolisms. Sarafoff (1930) mentioned 19 instances of embolism after fractures in reporting 95 fatal embolisms, 88 of which were verified by autopsy.

A review of the necropsy records in the Department of Pathology of the University of Minnesota for the period January 1, 1927, to July 1, 1933, revealed 9,781 cases which are suitable for analysis from the standpoint of pulmonary embolism. The postmortem records of stillbirths, newborns in whom no adequate cause of death was found, and partial examinations were rejected. Analysis shows that for the purposes of this paper 1,499 (15.3 per cent) were deaths from mechanical injury. Of the 1,499, 1,174 were males and 325 females, a ratio of 3.6 to 1. For the entire series of necropsy records examined the ratio of males to females is 1.7 to 1. For the entire series the incidence of pulmonary embolism is 2.8 per cent.

In the traumatic group, there were 61 pulmonary embolisms, an incidence of 4.0 per cent. In the non-traumatic group there were 222 embolisms, an incidence of 2.6 per cent. Statistically this appears to be a significant difference. Of 283 deaths due to pulmonary embolism, 61, or 21.6 per cent, followed trauma. In other words, 15.3 per cent of the cases analyzed accounted for 21.6 per cent of the fatal pulmonary embolisms.

The age distribution of the cases is about the same in the two groups. For the entire series studied the incidence of pulmonary embolism is 2.5 per cent in males and 3.6 per cent in females. This appears to be a significant difference. The greater incidence in females is not to be accounted for by the embolisms which followed childbirth (11 cases). The incidence of embolism after trauma is 2.8 per cent in the male and 8.6 per cent in the female. This difference is significant.

Four possibilities suggest themselves as explanations of this sex difference in the incidence of post-traumatic pulmonary embolism: (1) The age distribution of the cases may be different in the two sexes. (2) Heart disease may be more frequent in females than in males. (3) Perhaps more of the males died shortly after being injured, because of the greater liability to industrial accidents. (4) There may be anatomical differences in the blood vessels of the pelvis and lower extremities in the two sexes.

An analysis of these cases was made in an attempt to find answers to these possibilities. Table I shows the age distribution of the traumatic deaths by sex, by number, and percentage of cases and incidence of pulmonary embolism. From this table it appears that there was, on the whole, no very great difference in the age distribution in the two sexes, the first, fifth, and eighth decades showing the greatest discrepancies. On the other hand, the sex difference in the incidence of pulmonary embolism is very striking. It would appear that, in this series of cases, the difference in incidence of pulmonary embolism in the two sexes is not to be explained on the basis of age.

The series was then examined for the incidence of anatomical heart disease. It was found that

[1]Acknowledgment is hereby made of assistance received from the Civil Works Administration.

TABLE I.—AGE AND SEX DISTRIBUTION OF TRAUMATIC DEATHS AND PULMONARY EMBOLISMS

	Males				Females			
Decade	No. cases	Per cent	No. emboli	Incidence emboli per cent	No. cases	Per cent	No. emboli	Incidence emboli per cent
1	71	6.0			36	11.0		
2	59	5.0	1	1.7	23	7.0		
3	128	10.9			25	7.6		
4	127	10.8	2	1.5	40	12.3	2	5.0
5	167	14.2	4	2.3	25	7.6	2	8.0
6	158	13.4	7	4.4	38	11.6	8	21.0
7	182	15.5	11	6.0	49	15.0	6	12.2
8	121	10.3	8	6.6	50	15.3	6	12.0
9	43	3.6			17	5.2	3	17.6
10	1	0.08			1	0.3		
Adult	117	9.9			21	6.4	1	4.7
Total	1174		33	2.8	325		28	8.6

TABLE II.—AGE DISTRIBUTION OF DEATHS AND PULMONARY EMBOLISMS

	Traumatic				Non-traumatic			Total per cent of emboli-sms
Decade	No. of deaths	No. of emboli-sms	Per cent of emboli-sms		No. of deaths	No. of emboli-sms	Per cent of emboli-sms	
1	107				1116	2	0.1	0.1
2	82	1	1.2		327	2	0.6	0.7
3	153				613	13	2.1	1.6
4	167	4	2.3		871	26	2.9	2.8
5	192	6	3.1		1237	33	2.6	2.7
6	196	15	7.6		1326	45	3.3	3.9
7	231	17	7.3		1420	44	3.0	3.6
8	171	14	8.1		893	37	4.1	4.7
9	60	3	5.0		231	17	7.3	6.8
10	2				15	1	6.6	5.8
Adult	138	1	0.7		232	2	0.8	0.8
Total	1499	61	4.0		8281	222	2.6	2.8

heart disease was present in 20.5 per cent of the males and 18.4 per cent of the females. This obviously does not account for the sex difference in occurrence of pulmonary embolism.

Since no patient died of pulmonary embolism within the first 24 hours after being injured (Table V) the series was examined after eliminating the deaths occurring during this period of time. This procedure left a total of 722 cases—552 males and 170 females—to be studied. The incidence of pulmonary embolism was then 5.9 per cent in males and 16.4 per cent in females. These 722 cases were then studied from the standpoint of the presence or absence of anatomical heart disease and the occurrence of embolism. This study revealed that the incidence of embolism was, in the non-cardiac group, 5.5 per cent in males and 13.6 per cent in females, and in the cardiac group 7.1 per cent in males and 24.9 per cent in females. No help in explaining the sex difference in incidence of pulmonary embolism was obtained by these analyses.

This series of cases did not lend itself to analysis from the standpoint of attempting to answer the fourth of the above stated possibilities. So far as I can learn there are no normal anatomical differences in the blood vessels of the pelvis or lower extremities which might account for the sex difference in incidence of post-traumatic pulmonary embolism. However, it is well known that varicose veins are much more frequent in females than in males after the age of 20 years. McPheeters (1931) gives the ratio of varicose veins as 4 in the female to 1 in the male. Unfortunately, the present series gives no clue as to the frequency of varicose veins, but it is reasonable to assume that diseased vessels would be more susceptible to trauma than normal ones. It may well be that the real explanation for the higher incidence of post-traumatic pulmonary embolism in females is this greater frequency of varicose veins.

The distribution of deaths and embolisms by decades and the incidence of embolisms in the various decades is shown in Table II. It is apparent that in both groups, the maximum incidence of pulmonary embolism is between the ages of 50 and 80 years, although it may occur at any age. The wider age distribution of embolisms in the non-traumatic cases is apparent.

Table III shows the same findings somewhat more clearly by percentages. In persons of known age in the traumatic group 75 per cent of the cases occurred in this age period, whereas in the non-traumatic but 57.2 per cent were in the same period.[1] The great importance of age in the causation and occurrence of embolism is very clearly brought out in these tables. It is probably not merely the age that is of importance but rather

[1] Comparison of this table with one given in my previous paper shows no agreement at all in the decade distribution of embolisms. The present findings are more nearly in agreement with those of other authors than the earlier table. It appears that my statement, "This suggests that age is not as important a factor as is commonly supposed," was incorrect, since from the present table age is obviously an extremely important factor in the occurrence of embolism. A possible explanation for the discrepancies in the two tables may lie in the increased care used in the search for emboli in the more recent autopsies.

TABLE III.—AGE DISTRIBUTION OF PULMONARY EMBOLISM BY PERCENTAGES OF EMBOLISMS

Decade	Traumatic	Non-traumatic	All cases
1		0.9	0.7
2	1.6	0.9	1.0
3		5.8	4.5
4	6.5	11.7	10.6
5	9.8	14.8	13.7
6	24.5	20.2	21.2
7	27.8	19.8	21.5
8	22.9	16.6	18.0
9	4.9	7.6	7.0
10		0.4	0.3
Adult	1.6	0.9	1.0

the accompaniments of age, viz., the decreased muscular activity with resulting impaired tone of the muscles, the high incidence of cardiac disease, the tendency to obesity, the greater incidence of debilitating disease, etc., all of which tend to slow up the circulation.

Inasmuch as there are almost no large series of cases of post-traumatic pulmonary embolism recorded, I believe that as detailed a description of such a series as space will permit may be of value. It is realized that many defects exist in individual cases of this series and that if the data were available their usefulness would be greatly increased.

CASE REPORTS

CASE 1. (31–24.) A fairly well nourished female, aged 52 years, had sustained an intracapsular fracture of the right femur, 35 days before death. Four or five days before death she had a sudden attack of dyspnea, cyanosis, and pain in the chest. There was bloody sputum on coughing. She recovered from this attack. Death took place suddenly. Autopsy findings: embolus in main pulmonary artery; infarct in left lung; thrombosed right common iliac vein; heart normal (257 grams).

The symptoms appearing 4 or 5 days before death should have made one suspect embolism. This was probably the time when the infarct in the right lung developed.

CASE 2. (32–2038.) Patient was a poorly nourished female, aged 52 years. She had fallen 25 days before death and had fractured the neck of the left femur. She was treated by traction and Jones splint. She got along well until the day before death when the leucocyte count was found to be 15,000. The day of death the temperature was 104 degrees. The manner of death was not described. Autopsy findings: embolus in artery of right lower lobe; thrombosed left femoral, external iliac and saphenous veins; edema of the left knee; bronchopneumonia; heart normal (190 grams).

CASE 3. (32–1664.) A fairly well nourished male, aged 52 years, had fallen downstairs 8 days before death, sustaining an impacted intracapsular fracture of the left femur. His course was satisfactory; the temperature never rose above 99.2 degrees; the leucocyte count was 10,000. Three minutes before death he had an attack of moderate cyanosis and an epileptiform seizure. There was no sign of chest pain. Autopsy findings: embolus in main pulmonary artery; free thrombus in vena cava; thrombus in region of fracture and *right* common iliac vein; questionable edema of right leg; heart normal (355 grams).

TABLE IV.—TYPES OF INJURY WITH NUMBER OF CASES AND INCIDENCE OF PULMONARY EMBOLISM

Fractures	No.	P.E.	Per cent P.E.
Skull	435	1	0.2
Ribs	109	2	1.8
Spine	68	1	1.4
Arm	25	2	8.0
Pelvis	31	1	3.2
Tibia and/or fibula	39	8	20.5
Femur	118	27	22.8
Multiple bones	251	13	5.1
Gunshot	134	..	..
Miscellaneous trauma	289	6	2.0
Total	1,499	61	4.0

It is to be noted that in this case there were two possible sources for the embolus, one in the region of the fracture and one on the opposite side. One may be an extension of the other. It is also possible that there was deep bruising of the right side, although none was described.

CASE 4. (29–674.) Patient was an obese female, aged 55 years. She had collided with another pedestrian and fell, fracturing the neck of the right femur, 3 days before death. Some hours before death she became cyanotic and dyspneic and appeared to be in shock. Autopsy findings: emboli in both lungs; antemortem blood clot milked from veins of right lower extremity; heart enlarged (450 grams).

CASE 5. (30–946.) Patient was a well nourished female, aged 58 years. She had fallen 36 days before death, suffering a subcapsular fracture of the left femur. A cast was applied. About 1 week after application of the cast there developed a painful phlebitis of the superficial veins of the *right* thigh. On the second, third, fourth, and eighteenth to twenty-third days the temperature rose to 101 degrees. There were slight rises on the twenty-ninth and thirty-third days. Several days before death she suffered from severe dyspnea. Death took place "quite suddenly." Autopsy findings: bilateral pulmonary embolism; infarct of left lung; thrombosis of *right* common and external iliac, femoral and greater saphenous veins; veins of left lower extremity normal; edema of right leg; heart normal (300 grams).

This is an exception to my statement that the source of the embolus is always in the region of the trauma. The non-fatal embolism with infarct formation apparently took place several days before death at the time of the "severe dyspnea." This should have served as a warning of the danger of the occurrence of a fatal embolism.

CASE 6. (30–201.) Patient was a well nourished male, aged 61 years, who, 10 days before death, sustained a dis-

TABLE V.—TIME OF PULMONARY EMBOLISM AFTER TRAUMA

61 Cases

Interval	Cases	Total
3 days	2	..
4 days	2	..
5 days	2	..
6 days	2	..
7 days	1	..
Second week	21	30
Third week	10	..
Fourth week	6	..
Later	15	31
Total cases		61

location and fracture of the head of the right femur. Several attempts were made to reduce the fracture. On the day of death, under spinal anesthesia, reduction was accomplished and a cast was applied. While still on the table, he suddenly became cyanotic. (Was the manipulation responsible for the loosening of the thrombus?) Autopsy findings: embolus in right pulmonary artery; thrombosed right iliac vein; bruising of both thighs, especially the right; heart normal (400 grams).

CASE 7. (31–2032.) The patient, an obese female, aged 63 years had been in an automobile accident 8 days before death, and had sustained fractures of both femurs and laceration of the forehead. X-ray examination revealed comminuted fracture of head and lower half of right femur. The day before death the right femur was manipulated and a Steinmann pin was inserted. Subsequently she complained of pain in this leg. She grew weaker and her respirations more rapid. She became semistuporous and later comatose. Autopsy findings: bilateral embolism of the pulmonary arteries; infarcts in both lungs; source of emboli undetermined; carotid artery embolus (?); heart normal (368 grams).

This case is included in the group of fractures of the femur rather than in the group of multiple fractures in Table IV. This patient showed none of the usual symptoms of pulmonary embolism.

CASE 8. (32-1129.) An obese male, aged 65 years, had fallen 13 days before death, and had sustained a transverse fracture of the middle third of the right femur. Traction was applied. Six days before death he began to complain of pain in the right thigh. Four days before death, ether was administered for the application of calipers. Course was "quite satisfactory." His temperature varied from 98 to 101 degrees. There was a sudden attack of dyspnea with marked cyanosis, but no pain. He was dead in 2 minutes. Autopsy findings: embolus 15 by 1 centimeter picked from the pericardial sac following removal of the heart; infarct of the right lung; thrombosed right internal iliac vein; heart hypertrophied (475 grams).

The embolism which was responsible for the infarction of the right lung apparently gave no symptoms. The finding of well developed infarcts in the lungs is rather frequent in cases of suddenly fatal embolism, although the earlier non-fatal embolism may not have caused symptoms.

CASE 9. (31-1687.) The patient who was a well nourished female, aged 65 years, about 6 weeks before death had suffered a compound fracture of the lower third of the right femur involving the knee joint. The knee was incised 3 times, 6 weeks, 2 weeks, and 8 days before death, and pus was obtained. Transfusion was done twice. Leucocyte count was 21,400; polymorphonuclears 82 per cent. Temperature ranged from normal to 103 degrees. Blood pressure was 136/96. She was stuporous most of the time. Autopsy findings: gas gangrene; right thigh swollen, showing several sinuses filled with thick creamy pus; gas bacillus septicemia; multiple small emboli in both lungs; source not found; infarct of right lung; chronic passive congestion of lungs; heart normal (240 grams).

CASE 10. (30-962.) A fairly well nourished female, aged 67 years, had fractured her right femur 52 days before death. Her course was favorable until sudden death. Autopsy findings: bilateral pulmonary embolism; thrombosed right femoral vein and veins in bruised area about fracture; heart, coronary sclerosis (350 grams); edema of right leg; right thigh larger than left.

CASE 11. (30-1622.) A fairly well nourished female, aged 68 years, had fractured her left femur 4 weeks before death. The left leg was bruised. A cast was applied. The progress was favorable for a time. Later she complained of dizziness and nausea. Subsequently, she went into coma. During the last 36 hours, there were diarrhea and cramps. Systolic blood pressure was 200. She was a diabetic with blood sugar, 0.185. Autopsy findings: pulmonary embolism; infarcts in both lungs; edema of left leg; bruise of left leg; source of embolus not found; heart showed hypertension and coronary sclerosis (400 grams).

The symptoms, together with the hypertension and diabetes mellitus, might well have suggested a cerebral accident or diabetic coma rather than pulmonary embolism.

CASE 12. (30-1025.) A well nourished male, aged 69 years, 13 days before death had fractured the neck of the left femur, and had bruised the soft tissues. About 24 to 36 hours after the fracture he became delirious and had a temperature of 101.5 degrees. Autopsy findings: bilateral pulmonary embolism; thrombosed left femoral vein; bronchopneumonia; heart normal (400 grams).

CASE 13. (31-1786.) An obese female, aged 69 years, was in an automobile accident 19 days before death, and had suffered an intertrochanteric fracture of the left femur, lacerations of the scalp, concussion (?). She was unconscious for a short time. Her course was afebrile and favorable. She died suddenly. Autopsy findings: embolus in main pulmonary artery and the large branches—source not found; heart normal (345 grams).

CASE 14. (32-154.) A poorly nourished male, aged 69 years, fell 21 days before death, producing an intracapsular fracture of the left femur. A cast was applied. Twelve days antemortem he had rusty sputum; later it was bloody. He had sharp pain in the right lower chest with dullness and râles. Temperature was normal. Diagnosis: bronchopneumonia. Later temperature rose to 101 degrees. Nine days before death, temperature was 103 degrees. The day of death he had a chill; his temperature was 104.8 degrees. Autopsy findings: bilateral embolism; embolus partially adherent but folded—source not found; edema of right leg and thigh; heart normal (350 grams).

The symptoms, complained of 12 days before death and diagnosed "bronchopneumonia," may well have been those of embolism with infarction. At necropsy neither bronchopneumonia nor infarction was found.

CASE 15. (32-1544.) Patient was a well nourished male, aged 69 years. He fell 14 days before death, fracturing the left femur. Death was sudden. Autopsy findings: embolus in main trunk of pulmonary artery; thrombosed left femoral vein in region of fracture; heart normal (350 grams).

CASE 16. (27-652.) A poorly nourished female, aged 70 years, fell 122 days before death, fracturing the right femur. Her blood pressure was 134/22. The day of death she was up on crutches. She had an attack of weakness and coldness; collapsed and died in about 3 minutes. Autopsy findings: main and bilateral embolism, partially adherent; thrombophlebitis of right leg; edema of right leg, thigh and left ankle; heart normal (271 grams).

CASE 17. (30-43.) Patient was an emaciated female, aged 72 years. She fell 18 days before death, sustaining an impacted intracapsular fracture of the neck of the left femur. Taking advantage of the enforced rest, she had a facial tumor removed on the day of death. There was difficulty in breathing at the start of the operation (local anesthesia). She died suddenly the same day. Autopsy findings: embolus right pulmonary artery—source not found; chronic passive congestion of lungs; heart normal (310 grams).

CASE 18. (28-1019.) The patient, a fairly well nourished male, aged 73 years, fell 93 days before death, suffering a fracture of the neck of the left femur. It was treated by traction. Two days after the fall the leucocyte count was 19,100; 1 month later 27,000. He was up and about 3 days before death, feeling well. While walking he suddenly fell over and died. He had hypertension and the blood pressure was 204/90. Autopsy findings: embolus in left pulmonary artery; thrombosed left femoral and hypogastric veins; edema both lower extremities, especially the left; heart, hypertension (350 grams).

CASE 19. (30-1004.) Patient was a fairly well nourished male, aged 73 years. He fell 13 days before death, sustaining a comminuted fracture of the left femur extending into the knee joint. Treatment consisted of extension and application of a Thomas splint. The extremity was manipulated 4 days before death; a Steinmann pin was put in 3 days before death under nitrous oxide anesthesia. Two days before death he vomited decomposed blood; had a chill, temperature of 103 degrees; pulse of 140; was cyanotic and stuporous; but had no pain. One day before death abdominal distention developed; temperature normal. One and one-half hours antemortem he had chill, weakness, cyanosis, and thready pulse. Axillary temperature was 105.8 degrees. Autopsy findings: small bilateral pulmonary emboli; antemortem clot which was milked from veins of left lower extremity; edema of left lower extremity; heart, coronary sclerosis and myocardial fibrosis (425 grams).

CASE 20. (33-296.) Patient was a well nourished female, aged 74 years. She fell 25 days before death, suffering a fracture of the left femur. Blood pressure was 148/78. Forty-two hours before death she became restless and unresponsive; had twitchings of hands and arms, cyanosis, stertorous respirations, pulse rapid and feeble; incontinent (history of similar attacks in the past). These symptoms continued until death. Temperature was 102 degrees. The day of death she became weaker; respirations shallow and irregular, at times of Cheyne-Stokes type. Autopsy findings: embolus in main pulmonary artery; thrombus milked from left femoral vein; heart, pericardial space obliterated (375 grams).

The symptoms in this case suggest some cerebral lesion rather than pulmonary embolism. Cerebral symptoms are not rare in pulmonary embolism.

CASE 21. (29-375.) A moderately nourished male, aged 74 years, fell 5 days before death, fracturing his right femur through the trochanters. A cast was applied. The blood sugar was high. The night before death the temperature was 100 degrees. Death was rather sudden. Autopsy findings: multiple small emboli; thrombus milked from veins of right lower extremity; heart normal.

CASE 22. (28-27.) A well nourished male, aged 75 years. He fell 15 days before death and sustained a comminuted fracture of the left hip and a simple fracture of the lower third of the left femur. A cast was applied. Thirty-six hours antemortem cyanosis, marked respiratory difficulty, and congestion of the lungs developed. He improved after a few hours. Sudden death occurred the next evening. Autopsy findings: emboli in both lower lobes; embolus in vena cava from diaphragm to tricuspid valve; thrombosed left femoral vein; heart, calcified aortic valve defect (425 grams).

CASE 23. (31-414.) A fairly well nourished female, aged 75 years, fell out of bed 9 days before death, suffering a comminuted intertrochanteric fracture of the right femur. Temperature varied from 99 to 102 degrees. Two days antemortem she became unconscious. Blood pressure was 150/80. Autopsy findings: embolus in right pulmonary artery; thrombosed left common iliac vein and vena cava; encephalomalacia with hemorrhage; abrasions of right knee and thigh; bronchopneumonia; heart normal (347 grams).

Perhaps objection might be made to this case as an embolic death, since cerebral softening and hemorrhage were present. These intracranial lesions undoubtedly caused the unconsciousness. The manner of death was not described. There was pulmonary embolism, whether or not it caused death.

CASE 24. (32-142.) A poorly nourished female, aged 77 years, fell 83 days before death, sustaining an intertrochanteric fracture of the right femur. A cast and Jones splint were applied. She gradually grew weaker. Several days before death the respirations became labored. Autopsy findings: embolus left pulmonary artery; thrombosed right and left femoral veins; secondary acute tricuspid bacterial endocarditis (290 grams).

In this case there were three possible sources for the embolus in the lung. Which one was the source was not determined. The presence of tricuspid endocarditis suggests that in this case infection may have played a part in the development of the bilateral femoral vein thrombosis.

CASE 25. (32-682.) A poorly nourished female, aged 80 years, fell 17 days before death, and suffered a fracture of the right femur. Hypertension was noted with blood pressures 170/88, 206/78, 260/140. She had had edema, dyspnea, palpitation, and weakness for 1½ years. Two weeks antemortem she showed edema and marked dyspnea. There was progressive weakness. The temperature was normal except for a terminal rise. Autopsy findings: bilateral small emboli; infarct right lung—source not found; bronchopneumonia; heart, hypertension (380 grams).

It is indeterminate in this case whether the symptoms were due to hypertension or embolism. The infarct apparently gave no sign of its presence.

CASE 26. (28-1183.) A fairly well nourished female, aged 85 years, fractured the neck of the left femur 13 days before death. Hypertension was noted with blood pressure 185/100; shortness of breath; edema. She gradually grew weaker, and apparently died of heart failure. Autopsy findings: small emboli in left lung—source not found; edema, especially of left leg; chronic passive congestion of liver; heart, hypertension (330 grams).

It may be argued that this death should be charged to the decompensated heart disease and not to the pulmonary embolism and that the embolism is a complication of decompensation and is of the nonfatal form.

CASE 27. (27-526.) A poorly nourished female, aged 80 years, had fallen 3 weeks before death, sustaining a dislocation of the left femur. She became short of breath 4 days before death; cough 2 days with fever and bloody sputum; edema of ankles 1 week; heart enlarged to left; systolic murmur at apex; blood pressure 140/80. Autopsy findings: embolus right lower lobe—source not found; infarcts right lung; edema of ankles; chronic passive congestion of liver; heart, mitral and aortic valve defects, myocardial fibrosis (408 grams).

In Table IV this case is included with the fractures of the femur, because the local trauma and the type of treatment would undoubtedly be about the same as in fracture. Here again the part played by the heart disease and the embolism is indeterminate.

Seven other cases with fractured femurs might well have terminated with pulmonary embolism. A source for an embolus was found in each, but detachment of the thrombus did not take place.

CASE 28. (32-1879.) A fairly well nourished male, aged 75 years, fractured his right tibia and fibula 26 days before death. Cellulitis of the left arm developed following a burn suffered one or more days before death. Blood pressure was 130/80. He had labored respiration with shallow breathing. Autopsy findings: multiple small emboli; source not determined; edema of left arm; heart, mitral valve defect with acute rheumatic mitral endocarditis (400 grams).

The question may be raised whether the burn sustained played any part in the development of an undiscovered thrombosis and the resulting embolism.

CASE 29. (30-689.) A fairly well nourished male, aged 69 years, had a comminuted fracture of left tibia and fibula, sustained 29 days before death. It was plated 21 days before death. Patient had skin abscesses, clinical thrombophlebitis, osteomyelitis, and carcinoma of the prostate. Hypertension was noted with blood pressure 175/100. Temperature was 101 degrees, and cyanosis, weak rapid pulse, and distress were present. Autopsy findings: bilateral embolism; embolic pneumonia; thrombosed left common iliac and branches and left internal iliac veins; liver, chronic passive congestion; heart, hypertension; myocardial fibrosis (350 grams).

This case is rather complicated, because of the large number of pathological lesions present, and it is very difficult to determine what etiological rôle each played in the development of the thrombosis and embolism. The parts played by the trauma, the operation, the infection, the cardiac and the malignant disease in causing death are indeterminate.

CASE 30. (30-388.) A well nourished male, aged 44 years, sustained a comminuted fracture of the left tibia and fibula 50 days before death. Seven to 10 days before death he had bloody sputum. Death was rather sudden. Autopsy findings: embolus in main pulmonary artery and its large branches; infarcts in both lungs; thrombosed *right* external iliac and femoral veins and deep vein left lower extremity; heart, hypertrophied (?) (475 grams).

It is probable that the initial pulmonary embolism with infarction took place 7 to 10 days before death. The bloody sputum should have served as a warning of the possibility of a fatal embolism. Here again there are two possible sources for the emboli, one near the site of the fracture and the other in the opposite extremity. Whether there was also injury of the right lower extremity is unknown.

CASE 31. (32-1208.) A well nourished male, aged 46 years, fractured his right tibia and fibula 28 days before death. A Steinmann pin was inserted 25 days before death, and a cast was applied. Early in his illness he felt well and wanted to get up. Fifteen minutes before death he became very cyanotic, short of breath, and complained of his heart. Autopsy findings: embolus in main pulmonary artery; bilateral infarcts; thrombosed right femoral, right iliac, popliteal vein to area of fracture and vena cava; right lower extremity discolored and swollen; heart hypertrophied (?) (450 grams).

CASE 32. (29-1511.) An obese female, aged 53 years, fractured her right tibia 2 weeks before death. X-ray examination showed compression of lateral condyle of the tibia. Suppurative prepatellar bursitis developed. A cast was applied. Death was sudden. Autopsy findings: embolus in main pulmonary artery; thrombosed right popliteal vein; heart normal (300 grams).

CASE 33. (33-415.) A poorly nourished male, aged 62 years, fractured both tibias and fibulas in an automobile accident 16 days before death. Autopsy findings: small embolus of lower lobe of right lung; thrombosed vena cava and iliac veins; cerebral hemorrhage and encephalomalacia; heart normal (390 grams).

This case was grouped with the fractures of tibia and fibula in Table IV instead of with the multiple fractures, because the fractures were of the same bones even though bilateral. The question may be raised whether death should not be attributed to the brain injury rather than to the embolism.

CASE 34. (30-1317.) A well nourished male, aged 51 years, fell, 2 weeks before death, fracturing the lower end of the right fibula and the left os calcis. A cast was applied. Autopsy findings: multiple small emboli in both lungs; thrombus milked from right lower extremity; bronchopneumonia; edema of left foot and ankle; heart normal (375 grams).

This case was grouped with the fractures of the tibia and fibula instead of with the multiple fractures (Table IV).

CASE 35. (30-749.) A well nourished female, aged 33 years, fractured her right pubis 11 days before death. She also had bleeding from the right ear. She was apparently recovering until about one-half hour before death, when dyspnea and cyanosis developed and her pulse became weak. Autopsy findings: embolus in main pulmonary artery; thrombosed *left* femoral vein; ecchymoses of right elbow, shoulder, and hip; heart normal (260 grams).

This is another exception to my statement that the thrombus always develops near the site of fracture. However, it is to be noted that there was ecchymosis over the right hip and there may have been deep injury, although none was described.

CASE 36. (30-1485.) A well nourished male, aged 53 years, 4 days before death, fractured his skull and suffered as well laceration of the forehead. Autopsy findings: embolus in right lung; infarct of left lung; source of emboli not found; bronchopneumonia; heart normal (340 grams).

Unfortunately the source for the embolus was not found in this case. It is possible that the source might have been in a dural sinus. In this series of traumatic deaths there were 435 fractures of the skull and in 6 of these thrombi were found in the dural sinuses. These 6 may be considered as cases of potential pulmonary embolism.

CASE 37. (32-2012.) An obese male, aged 60 years, fractured a vertebra, 44 days before death, and suffered abrasions of the forehead. He had pain in the neck and numbness of the right arm. Blood pressure was 150/90. X-ray examination revealed dislocation of fifth on sixth cervical vertebras. A cast was applied. Course was uneventful. He suddenly complained of severe pain, with respirations, slow and deep; pulse, weak; no cyanosis. Cardiac type of death. Autopsy findings: multiple small emboli or thrombi —source not found; heart normal (405 grams).

CASE 38. (29-1137.) A well nourished male, aged 67 years, fell 11 days before death, fracturing three ribs on the left side. There was a bruise over the left greater trochanter and one on the back of the right shoulder. The chest was strapped. After breakfast he had an attack of difficult breathing and died at 9 a.m. Autopsy findings: embolism of left lung—source not found; bronchopneumonia; heart, coronary sclerosis (400 grams).

CASE 39. (27-920.) A fairly well nourished male, aged 49 years, was thrown from a wagon 16 days before death, and suffered fractures of the ribs on both sides, fracture of the eleventh dorsal vertebra, bruise of left breast. Subcutaneous emphysema was noted and pneumothorax. Leucocyte count was 6,250. Temperature was 99 to 104 degrees. The condition was good 25 minutes before death. Ten minutes before death he became cold, clammy, pulseless and dyspneic. Autopsy findings: embolism of right lung; thrombosed left common iliac vein; heart normal (330 grams).

Here the source of the embolus was well removed from the sites of obvious injury.

CASE 40. (27-1123.) A well nourished female, aged 72 years, had fractured some ribs and her right leg, 13 days before death. The tibia and fibula were plated. Death was sudden. Autopsy findings: bilateral pulmonary embolism; thrombosed right popliteal vein in region of fracture; heart normal (300 grams).

CASE 41. (28-1524.) Patient was a well nourished male, aged 78 years. Eleven days before death he had fractured some ribs on the right and bruised his right leg. A bruise was present in the lumbar region. The chest was strapped. Autopsy findings: bilateral embolism; thrombosed right femoral vein; bronchopneumonia; heart, coronary sclerosis (425 grams).

It should be noted that there was bruising but no fracture of the right leg; nevertheless it was in this extremity that the thrombosed vein was found.

CASE 42. (29-1019.) Patient was a well nourished female, aged 67 years. Six days before death she fractured the left pubis and ribs on the right. Large varicose veins were present on right leg. She was afebrile. Fourteen and one-half hours before death she went into shock. Blood pressure was 150/80. Autopsy findings: bilateral embolism; thrombus milked from left lower extremity; thrombosed left common iliac vein; heart normal (350 grams).

This patient had varicose veins of the *right* leg but the thrombosed vein was found on the *left* side, fairly close to one of the sites of bone fracture.

CASE 43. (30-1063.) A well nourished female, aged 46 years, had fractured her left clavicle and ribs 15 days before death. She was taken home from the hospital 4 days before death. Death was "quite sudden." Autopsy findings: embolus in main pulmonary artery—source not found; heart normal (250 grams).

CASE 44. (30-1967.) An obese female, aged 55 years, was injured in an automobile accident 3½ days before death, sustaining fractures of the right humerus, tibia, and ribs; laceration of forehead; bruising of both knees and right leg. A splint was applied. While splint was being removed she complained of difficulty in breathing and died in about 10 minutes. Autopsy findings: small emboli in both lungs; thrombi in both external iliac veins and inferior vena cava; heart hypertrophied (520 grams).

CASE 45. (31-678.) A well nourished male, aged 55 years, fell, 7 days before death. The X-ray revealed fractures of left os calcis and both wrists; compression fracture first lumbar vertebra; separation of left sacro-iliac joint and symphysis pubis. Urine was bloody. He became irrational 2 days before death. Six hours before death he had sharp pain in the right chest and dullness over the middle lobe. Ten minutes before death he developed severe sharp pain beneath the upper portion of the sternum and became extremely cyanotic, with gasping respirations and engorgement of neck veins. Autopsy findings: embolus in main pulmonary artery; infarct right lung; thrombosed left femoral vein; heart normal (380 grams).

CASE 46. (31-1634.) Patient was a well nourished male, aged 31 years. He was injured in an automobile accident, 26 days before death, when he sustained fractures of the left scapula and 4 ribs; laceration and bruises of the scalp; with bruising of the right upper arm and the left knee. Eighteen days before death a diagnosis was made of pneumonia. There was difficult respiration and a temperature of 99 to 101 degrees. The X-ray showed a left hydropneumothorax. Sixteen days before death temperature was

102.5 degrees. Six days before death the leucocytes were 18,000. Four days before death there was a sudden attack of syncope with air hunger and thready pulse. Three days before death the chest was aspirated and air injected. The following day the leucocytes were 23,200. About 15 minutes before death he had abdominal pain, anxiety, air hunger, and then syncope. Autopsy findings: bilateral pulmonary embolism and thrombosis; emboli found in right heart and inferior vena cava; infarct of left lung; thrombus milked from left common iliac vein; bronchopneumonia; heart normal (345 grams).

In this patient there was bruising of the left knee, which may account for the thrombus which was milked from the left common iliac vein. Where this expressed thrombus was attached is unknown.

CASE 47. (32-1493.) A well nourished male, aged 67 years, was injured in an automobile accident 14 days before death. X-ray examination revealed a comminuted fracture of left tibia, extending into knee joint; fracture of neck of left femur and greater trochanter; bruise of left wrist; abrasions and laceration of left hip. Twenty-four hours before death temperature rose to 105 degrees. Pulse was 90 to 130. Autopsy findings: small embolus or thrombus in right pulmonary artery—source not found; lobar pneumonia; heart normal (354 grams).

CASE 48. (33-305.) A well nourished female, aged 46 years, was in an automobile accident 9 days before death with resulting fractures of pelvis, right clavicle, ribs (both sides), and a bruise of the right shoulder. She was getting along well when she suddenly became cyanotic. Autopsy findings: bilateral pulmonary embolism—source not found; heart normal (285 grams).

CASE 49. (31-1702.) A well nourished male, aged 18 years, was injured in an automobile accident 13 days before death, sustaining compound fractures of the left humerus and radius. He got along well. While eating, sitting in bed, he complained of his heart, "it had stopped beating." Autopsy findings: embolus in main trunk and both branches of pulmonary artery; thrombosed left basilic vein; heart normal (300 grams).

This case is of interest for two reasons: first, because all other patients dying of post-traumatic pulmonary embolism were at least 30 years of age; second, because the embolus followed fracture of an upper extremity, which is rare. Whether the fact that the fractures were compound had any rôle is open to question, since in most instances of post-traumatic pulmonary embolism the fractures are not compound.

CASE 50. (27-269.) A well nourished female (adult), 13 days before death, had suffered bilateral fractures of ribs and left clavicle. There was bruising of the left shoulder, knee, and both legs. Sixty-eight minutes before death she had precordial pain, cyanosis, and dyspnea. Pulse was 132. She went into shock and became cold and clammy. The temperature was subnormal. There were râles and bronchial breathing. Autopsy findings: bilateral pulmonary embolism; thrombus milked from left leg; subarachnoid hemorrhage; heart, pericardial space obliterated (283 grams).

It is to be noted that there was merely bruising of one knee and both legs.

CASE 51. (31-443.) A fairly well nourished male, aged 59 years, was in an automobile accident 53 days before death, sustaining fractures of the right leg and left ribs. In the hospital he was semicomatose and had fever. Autopsy findings: bilateral pulmonary embolism; infarcts of left lung; thrombosed left iliac and femoral veins and vena cava; bronchopneumonia; heart, coronary sclerosis (300 grams).

This case suggests propagation of the thrombus to make it bilateral.

CASE 52. (31-87.) A well nourished male, aged 40 years, fell, 4½ days before death, with production of a compound comminuted fracture of the lower third of the right femur and fracture of ribs on the right. A splint was applied. He got along well until 2 days before death when gas gangrene was noted. The infected tissue was excised on the day before death. Autopsy findings: embolism of left lung—source not found; heart, subacute bacterial endocarditis of mitral valve (384 grams).

Did the facts that the fracture was compound, that gas gangrene was present, and that the infected tissue was excised have anything to do with the embolism?

CASE 53. (29-910.) A well nourished male, aged 36 years, 5 days before death, sustained compound fractures of right ankle and left humerus, fractures of nose and right ribs. Cellulitis of right leg developed. The ankle was operated upon on the day of death. There was a septic type of temperature. The day of death the temperature was 100.6 degrees; he felt well. Symptoms of embolism appeared 70 minutes before death. Autopsy findings: small embolus left lung; infarct (?) right lung; thrombosed vein of right leg; cellulitis left ileopsoas muscle; edema of right leg; heart normal (300 grams).

What parts did the compound nature of the fractures and the cellulitis play in the development of the thrombus?

CASE 54. (28-1481.) A well nourished male, aged 65 years, was injured in an accident 6 days before death, the injury sustained demanding amputation of the left leg at the knee. He had a bruise of the right upper arm, and signs of pulmonary edema. Autopsy findings: small bilateral emboli; thrombosed left femoral vein; heart normal (285 grams).

This is classified with fractures of the tibia in Table IV.

CASE 55. (32-469.) A fairly well nourished male, aged 79 years, was injured in a motorcycle accident 4½ months before death, suffering a bruised face. Later a nasal infection developed. Three days before death he was up and around. Suddenly he developed a severe pain in the left chest with cyanosis and cough. Later there were fever and râles. Autopsy findings: "bilateral adherent emboli"; infarcts left lung; thrombosis in prostatic plexus; heart normal (425 grams).

One might possibly object to the inclusion of this case on two grounds: first, that the trauma is too long removed and was too slight and that the nasal infection was the most likely cause; and, second, that it should be regarded as pulmonary

thrombosis instead of embolism. These objections are difficult to deny.

CASE 56. (33-1082.) An obese female, aged 50 years, received lacerations of the right forearm in an automobile accident 2 weeks before death. She had hypertension. Six hours before death there developed dyspnea and pain in the head, the pulse was very weak, and breathing was heavy. Autopsy findings: "pulmonary embolism or thrombosis"; thrombosed veins right forearm; edema of legs; heart hypertrophied (575 grams).

This case somewhat resembles Case 49, although there was no fracture.

CASE 57. (33-776.) An obese female, aged 50 years, fell down stairs 16 days before death and ruptured her spleen. She was unconscious for a few minutes and semicomatose for 12 hours. There was pain in the left abdomen and flank. Abdominal distention and dyspnea developed. Systolic blood pressures were 70, 130, and 140. Twelve days before death the leucocytes were 21,500; polymorphonuclears, 74 per cent. Four days before death the temperature was normal. There was soreness of left shoulder, chest, and buttocks. Forty-eight minutes before death there was sudden difficulty in breathing, gasping respirations, cyanosis, skin cold and clammy. Autopsy findings: embolus in main pulmonary artery—source not found; heart, left ventricular hypertrophy (475 grams).

CASE 58. (28-1266.) An obese male, aged 54 years, fell 9 days before death, scraping the calf of the right leg. There was brawny swelling and bluish discoloration of the right leg below the knee. It was treated by elevation, heat, and massage. About 24 hours before death he had difficulty in breathing and cyanosis. These lasted a few minutes. About 1 hour before death, during massage, he complained of a peculiar sensation, "His stomach turning over." This was followed by dyspnea, cyanosis, and perspiration. Pulse was very poor. About 5 minutes before death cyanosis increased. Autopsy findings: embolus in main pulmonary artery; infarcts in right lung; thrombosed right popliteal vein; heart hypertrophied, myocardial fibrosis (500 grams).

Did the massage have anything to do with the loosening of the thrombus?

CASE 59. (31-1875.) A fairly well nourished male, aged 70 years, was admitted to the hospital 57 days before his death with hemiplegia, senila dementia, and fracture of the left humerus. His course was progressively downhill with increasing weakness. Autopsy findings: bilateral pulmonary embolism; infarcts of lungs; thrombosed left femoral vein; edema of left leg; carcinoma of stomach with metastases; heart normal (300 grams).

It was not determined whether the fracture of the humerus was a pathological one. Here again the source of the embolus was at a distance from the site of trauma. It might be argued that the debility from the hemiplegia and the carcinoma were of as great importance as the fracture in causing the thrombosis and subsequent embolism.

CASE 60. (31-1110.) A poorly nourished female, aged 39 years. (Three months before death she had an oophorectomy.) She was injured in an automobile accident 36 days before death. Shortly afterward there was abdominal pain. Thirteen days before death, a diagnosis was made of intestinal obstruction and the following day laparotomy was done. Progressive downhill course was noted. Autopsy findings: "bilateral pulmonary embolism or thrombosis" (partially adherent); infarct right lung; thrombosed right common iliac and uterine veins; wound infected; carcinoma of stomach; heart normal (200 grams).

There are some objections to including this as an instance of post-traumatic embolism. It is not clear why the accident was followed by abdominal pain. There was no clue in the record as to the injury sustained. Perhaps it might be argued that the laparotomy was of more importance than the trauma.

CASE 61. (33-1012.) A fairly well nourished male, aged 57 years, was stabbed in the abdomen 112 days before death. Laparotomies were done on the one hundred and twelfth, sixty-ninth, forty-third, and second days before death. He failed rapidly after the last operation. Autopsy findings: "bilateral pulmonary embolism or thrombosis"—source not found; heart normal (295 grams).

Objection may also be made to including this case as an instance of post-traumatic embolism. It might be stated that a stab wound of the abdomen should be included with laparotomies, especially since there were no other injuries. The four subsequent laparotomies may have been of more importance than the trauma. Objection might also be made on the basis that this was an instance of pulmonary artery thrombosis instead of embolism, since no source for an embolus was found.

These cases and the controls are summarized in Tables IV and V. The most striking thing in Table IV is the high incidence of embolism after fractures of the long bones of the lower extremities. This is probably due to several factors:

1. Fracture of the femur is an affliction of advanced age. Of the 118 fatal fractures (1 a dislocation) of this bone 108 were in persons of 50 years of age or over. This is not quite so true of fracture of the lower leg, although 28 of the 39 individuals were 50 years of age or older. Eighteen of the 31 individuals with fracture of the pelvis were 50 or more years of age. Sixteen of the 25 persons with fractured arm were 50 years of age or over. Thirty of the 68 cases with fracture of the spine were 50 years of age or more.

2. Fractures of the lower extremity but especially of the femur require more prolonged rest in bed and stricter immobilization than fractures elsewhere.

3. There is a high incidence of anatomical cardiac disease, which was as follows: femur 45 per cent; leg 28 per cent; pelvis 29 per cent; arm 28 per cent; and spine 14 per cent. If consideration is given only to those over 50 years of age these figures become, femur 49 per cent; leg 32

per cent; pelvis 44 per cent; arm 37 per cent; and spine 23 per cent. This does not mean that all or even a large part of these persons had any clinical evidence of cardiac disease, but that many may have had a potential impairment of their circulation. In this series of 61 embolic deaths, anatomical heart disease was present in 22 cases or in 36 per cent, which is a higher incidence than for the traumatic group as a whole (20 per cent).

4. It is well known that there is a decided tendency for the source of pulmonary emboli to be found in the veins of the lower extremities and pelvis. It is obvious that the trauma to soft tissues attendant on fracture of the long bones of the lower extremity may readily bruise or lacerate the veins in this region, giving excellent possibilities for the development of thrombi on the injured endothelium. Mention has already been made of the possible but unproven rôle of varicose veins.

In addition to the foregoing, other at present unknown factors may play a part.

In a former paper I called attention to the fact that post-traumatic embolism tends to occur later than postoperative and post-partum embolism. This is further shown in Table V wherein 31 of the embolisms took place after the second week and 15 after the fourth week.

The part played by operative procedures secondary to the trauma sustained is indeterminate. It is probably true that valid objections might be made to the inclusion of some of these cases as embolisms, but I feel that they all help to make impressive the frequency of thromboembolic disease of the lungs as a result of trauma.

In my former paper certain general conclusions were drawn, which require only slight modifications at this time.

1. (a) Post-traumatic thrombosis and embolism are rather common. In fact embolism is more common following trauma than after conditions not involving trauma. (b) Embolism following trauma is decidedly more common in females than in males.

2. The source of the embolus is usually at the site of injury.

Further it may be concluded:

1. Fatal fractures of the lower extremities are afflictions of advanced age.

2. Fracture of the femur or leg is the most common cause of post-traumatic pulmonary embolism.

3. The prolonged immobilization and rest in bed necessary for repair of fractures of the long bones of the lower extremity promote stasis and the possibility of a resulting thrombosis. It is to be noted that in 35 of the 61 cases there was a fracture of the lower extremity and that in the remaining 26 cases there were fractures or bruises of the lower extremity in 13.

4. The trauma to vessels by fractures gives an ideal site for the initiation of thrombosis.

5. Injuries requiring less degrees of enforced inactivity are only rarely followed by pulmonary embolism.

6. Age, heart disease, and time of death do not explain the sex difference in incidence of pulmonary embolism following trauma.

7. The incidence of anatomical heart disease is significantly higher in persons dead of post-traumatic pulmonary embolism than it is in persons dead of trauma without embolism.

SUMMARY

Sixty-one cases of pulmonary embolism following trauma are reported. These represent more than 20 per cent of the deaths due to pulmonary embolism in a series of 9,781 necropsies. In about 80 per cent of these post-traumatic pulmonary embolisms there was injury of a lower extremity, usually a simple fracture. Pulmonary embolism is rare after fractures of bones other than those of the lower extremity. Embolism following trauma is decidedly more common in the female than in the male. This sex difference is not to be explained on the basis of age, the incidence of heart disease, or the time of death following the injury. It is suggested that the higher incidence of varicose veins in the female may be responsible.

Since this paper was prepared Vance has reported 60 cases of pulmonary embolism following trauma. Of his 60 cases 45 involved injury, chiefly fracture, of the lower extremity. (Vance, B. M. Thrombosis of the veins of the lower extremity and pulmonary embolism as a complication of trauma. Am. J. Surg, 1934, 26: 19–26.)

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TREATMENT OF THE ATONIC BLADDER[1]

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THE terms "atonic bladder" or "cord bladder" are generally accepted as referring to a condition of incompetence of the detrusor muscles of the bladder resulting from abnormal innervation. Although atony of the bladder is always secondary to some extravesical lesion, when it occurs as the result of disease affecting nerves supplying the bladder, it may, from a clinical standpoint, be regarded as primary. If this were granted, atony of the bladder resulting from obstruction at the vesical neck might be regarded as secondary. In some cases both obstruction and abnormal innervation are involved.

Although the function of the nerves involved in micturition and the mechanism of micturition are not exactly known, theories have gained general acceptance in which the parasympathetic or sacral nerves are regarded as contracting or emptying nerves, and the sympathetic or presacral plexus in control of the internal sphincter is regarded as a group of filling nerves. Impairment of the parasympathetic or emptying nerves will cause retention of urine.

The exact manner in which the so called internal and external sphincters of the bladder and urethra function during micturition is still undetermined. The internal sphincter is composed of smooth muscle and is supposed to be in a state of tonic contraction, relaxing automatically on the emptying of the bladder. Only when the pressure of overdistention becomes great enough is the contracted status of the sphincteric muscle overcome. The function of the internal sphincter was first regarded as of little importance, for it was shown that its destruction, which frequently occurred in suprapubic prostatectomy, was not followed by any disturbance in micturition or in control of the bladder. It was evident that the external sphincter sufficed to prevent incontinence. However, in recent years the part played by the musculature involved in the so called vesical neck, and generally referred to as the internal sphincter, has assumed greater importance. It is now recognized that unless the internal sphincter, and particularly its dorsal portion, is completely relaxed, micturition is impeded and retention of urine will result. Inability on the part of the sphincter to relax has been called dysectasia. Failure of co-ordination of the muscles that are situated at the vesical neck and that are involved in micturition has also been considered to be a factor in causing retention. Such inco-ordination has been called achalasia. Although it is possible that such dysfunction is closely related to dysectasia, and that the two result from similar causes, yet retention of urine is occasionally observed when the internal sphincter may appear to be normal, and when there is no gross evidence of fixation.

Sphincteric dysfunction may result from a variety of causes which may be roughly grouped under the headings of mechanical and neurogenous. Mechanical fixation of the sphincter may result from cicatricial changes in the sphincteric and perisphincteric tissues secondary to chronic infection. This is well illustrated by the retention of urine that so frequently is observed with a so called contracted vesical neck; often the sphincter is involved in cicatricial tissue so that it is unable to relax. Although prostatic hyperplasia may cause retention of urine as the result of obstruction in the prostatic tissues, the coincident sphincteric rigidity is probably a greater factor.

As the result of either chronic sphincteric dysfunction or mechanical obstruction, secondary atony of the detrusor muscles may develop. With marked retention of long standing, the atony may become so extensive that, although the obstruction is removed, contractile power returns only in part. Various methods have been attempted to determine the remaining degree of contractile power in the detrusor muscles, as

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Fig. 1. Typical round, smooth outline of atonic bladder.

well as the possibility of their becoming rehabilitated. Cystometric studies have been carried out by various observers, with varying degrees of success. Rose has maintained that the cystometer, if its readings are correctly interpreted, will give a valuable index to the actual and potential status of the detrusor muscles. It has been our experience that although cystometric data are often of corroborative value, they frequently fail to give the definite information desired. Another index to the potential contractile power of the detrusor muscles may be derived from injection of acetylcholine or mecholin. If the expulsive force of the bladder is definitely increased as the result of such injections, it is possible to assume that contractile power eventually will improve.

In recent years, we frequently have observed an interesting condition characterized by marked atony of the musculature of the bladder, with chronic retention of urine, in which evidence of prostatic obstruction could not be discovered on rectal examination, or by cystoscopy, and in which physical examination, including examination of the nervous system, gives negative results. When the catheter is introduced, marked reduction in expulsive force is evident. A cystogram may give an outline that is typical of so called atonic bladder (Fig. 1); that is, there is a smooth, round outline, instead of the irregularities of trabeculation usually observed with obstruction. On cysto-urethroscopy, the wall of the bladder will appear to be flabby and distended, with no trabeculation or other evidence of obstruction. Careful inspection may, however disclose evidence of cicatricial changes, with more or less contracture or lack of elasticity of the tissues of the internal sphincter and vesical neck. In other cases there may be slight hyperplasia of the sphincteric tissues. These conditions may be easily overlooked unless carefully observed, and in some cases it is necessary to use a retrograde lens. The tissue present is usually not enough to cause actual obstruction, but it apparently interferes with the physiological relaxation or co-ordination of the internal sphincter so as to cause urinary retention.

In treatment of this condition, an attempt should be made to remove the cicatricial or hyperplastic tissues at the neck of the bladder. The direct vision punch has proved to be admirably adapted to this purpose. It is frequently surprising how little tissue it is necessary to remove, often not more than a gram or two, to bring about the desired degree of relaxation. In order to restore vesical function, it will be necessary to remove every bit of abnormal tissue which can be seen in any portion of the vesical neck, so that it is smooth and on an even surface with the mucosa of the bladder.

The return of function of the musculature of the bladder is often slow, and several weeks or months may be required after operation before function is fully restored. Following operation it may be necessary to leave a retention catheter in the bladder for several days, and in some cases it is necessary to perform intermittent catheterization for several weeks. It will be seen that the intervals of catheterization will increase, and the amount of residual urine will decrease, as the contractile power of the bladder returns. During the interval of recovery, intramuscular injection of acetylcholine has, in some cases, seemed to act as a nerve stimulant. Occasional instillation into the bladder of 1 ounce (30 c.cm.) of 0.1 per cent to 0.2 per cent of an aqueous solution of gentian violet also will hasten the desire to void. In a few cases, complete relaxation of the sphincter is exceedingly difficult to accomplish. In some cases, relaxation is aided by postoperative dilatation, at regular intervals, with a Kollman dilator expanded to as much as 40 or 45 French. In an occasional case, a spastic condition may persist, justifying resection of the presacral nerves in an effort to overcome the neurogenous imbalance.

In the past 5 years we have observed 24 patients with atonic bladder of this type. Function of the bladders of 20 of these was completely restored by the freeing of the internal sphincter of cicatricial or hyperplastic tissue, by the use of

the transurethral punch. In 3 cases, although retention was overcome, complete normal function was not restored. In 2 cases, permanent normal function was established after resection of the presacral nerves. In case no abnormality of the internal sphincter can be discovered, evident failure of co-ordination may be remedied.

ATONIC BLADDER IN THE FEMALE

Because of differences in structure of the sphincter of the bladder in the two sexes, problems related to atony of the bladder in the female, are quite different from those related to the corresponding condition in the male. Although the sphincter has been described as consisting of external and internal fibers, still, from a functional standpoint, there is but a single sphincter. Atonic bladder in the female may result either from neurogenous or mechanical factors, or both. When innervation of the bladder is involved, the lesion may be localized either to the central nervous system or to the terminal nerves. With atony resulting from a lesion of a nerve, marked relaxation of the sphincter, and incontinence, are observed much less frequently in the female than in the male. The sphincter may be relaxed on urethroscopic examination, but sufficient contractile power remains, aided by accessory muscles, to prevent much, if any, leakage. Sympathetic neurectomy may be indicated as long as the sphincter is continent, and some contractile power of the detrusor muscles remains. The imbalance between the sympathetic and the parasympathetic innervation, as it affects the vesical sphincter, is usually not as marked in the female as in the male; yet marked increase in expulsive force has been observed in several so called atonic bladders following presacral neurectomy.

Mechanical factors involving the sphincter usually result from hypertrophy, cicatrization, or tumor. As a result of such obstruction, secondary atony of the musculature of the bladder may follow, from which complete recovery may be slow and is not always possible, even though obstructive factors are eliminated. Hypertrophy of the sphincter, causing retention of urine and secondary atony, is frequently observed. It may be due to nervous imbalance or to hyperplasia. Although it may not be easily recognized, as a rule evidence of sphincteric hyperplasia is visible on urethroscopic examination. When either of these factors is evident, incision into the sphincter, with forcible dilation, often will correct the condition. It has been our experience that in most of these cases it is necessary to remove several pieces of tissue from different portions of the sphincter, before sufficient relaxation of the sphincter can be secured. The danger of secondary insufficiency, with slight incontinence, must be risked, but usually this is overcome as the sphincter recovers its tonus. Intermittent catheterization may be indicated for a variable period following sphincterotomy, in order to help restore the tonus of the vesical wall. What is accomplished is not removal of actual obstructing tissue, but correction of sphincteric dysectasia, with restoration of sphincteric relaxation.

MISCELLANEOUS TYPES OF ATONY

Atony of the wall of the bladder may result from injury to branches of the pelvic nerves, caused in the course of operations on the bladder, lower part of the ureter, or rectum. We have observed such atony occurring in 2 cases following ureterectomy, with extensive resection of the adjacent portion of the vesical wall. Evidence of atony was localized to the adjacent portion of the bladder but was sufficient, in one case, to cause 150 cubic centimeters of residual urine. Subsequent compensatory hypertrophy of the intact neuromusculature reduced this to 30 cubic centimeters. It was very evident that in the course of the resection important parasympathetic fibers had been cut.

Atony of the bladder was frequently observed several years ago, following the Kraske type of operation for resection of the sigmoid. It was very evident that sacral nerves controlling the detrusor muscles of the bladder were sometimes destroyed in the course of the operation. In most instances the wall of the bladder recovered its contractile powers, at least in part. In other instances, the atony remained permanent. In recent years, modifications in the technique of posterior resection of the sigmoid have been made, which have largely obviated such injury to nerves. When injury occurs, intermittent catheterization or suprapubic drainage should be instituted without delay.

Amounts of residual urine, varying from 30 to 100 cubic centimeters, are occasionally observed in the presence of clinical evidence of senility, although no definite lesion can be demonstrated on examination of the nervous system. Rectal examination and cysto-urethroscopy may also fail to demonstrate any cause for the residual urine. Largely by exclusion, it would seem logical to infer that a lesion exists in the structures that innervate the bladder, related to the arteriosclerotic or senile changes existing in the central nervous system.

Fig. 2. Pyramidal outline of bladder frequently seen with obstruction. Irregularities are caused by trabeculation and cellules.

Fig. 3. Another outline of the bladder seen with obstruction. Irregularities are caused by trabeculation, cellules, and by diverticula.

So called hysterical retention of urine is often observed, although, curiously, not so often as in former years. In most cases it is apparently caused by a spastic condition of the sphincter, of functional origin, although secondary atony of the wall of the bladder may be noted in cases of long standing. Absence of the reflex pain that usually is observed with overdistention of the bladder is a curious feature, and must be explained on the basis of hysterical diminution in sensation.

In the treatment of atonic bladder, with evident imbalance of sympathetic and parasympathetic innervation, before considering presacral neurectomy, Learmonth has advised preliminary exploration of the lower vertebræ if there is any doubt as to the existence of vertebral or spinal abnormality. In some of these cases no somatic evidence of a neurogenic defect can be obtained. Among the local compressing agents are tumors, cartilaginous bands, meningocele, and bony spurs. Removal of such structures will, in favorable cases, permit restoration of vesical function. When imbalance of innervation is marked by accentuation of the hypogastric influence, presacral resection has resulted in restoration, or marked improvement, of vesical function in a sufficient number of our cases to demonstrate its practical value. The indications laid down by Learmonth, for operation for neuromuscular imbalance, are as follows: (1) clinical data must point to reduction of function of the pelvic nerves, but sufficient function must remain to permit some contraction; (2) the hypogastric nerves must be uninjured. In other words, it is inferred that the balance of vesical innervation is disturbed, and injured pelvic nerves are handicapped in their task by the braking action of normal hypogastric nerves. However, there must not be total paralysis in the distribution of the pelvic nerves, for, after the brake is removed, the residual expulsive force of the detrusor muscles must become equal to emptying the bladder. In addition, the patient must be continent and must have no impairment of the external sphincter muscle, and finally, renal function must be satisfactory.

Presacral neurectomy is, unfortunately, not applicable in the majority of cases in which there are lesions of the central nervous system, such as there are in tabes. However, when the external sphincter is intact, and some residual contractile power remains in the detrusor muscles, presacral neurectomy may be considered. The atonic condition of the bladder of many tabetic patients will improve following antisyphilitic treatment, particularly if treatment includes intermittent catheterization. The amount of residual urine, perhaps originally large, will be greatly reduced by such treatment and in some cases all residual urine will disappear. It is of interest that atony of the bladder secondary to tabes occurs much less

frequently in the female. Presacral resection is rarely possible as a means of treatment of paralysis of the bladder following traumatic injury to the spine. As a rule, the contractile power of the detrusor muscles is completely lost, and even though the sphincter is intact, much cannot be expected from overcoming the braking influence of the sympathetic nerves.

The non-surgical treatment of atonic bladder is of considerable importance. Particular emphasis should be laid on drainage. We are inclined to agree with Cabot, that in every case in which acute retention occurs after operation or as the result of obstruction, the catheter should be employed to drain the bladder before its normal capacity is exceeded. Early and repeated catheterization will prevent renal infection better than any other measure. Whether or not suprapubic drainage is done is of secondary importance. The main objective is to prevent overdistention of the bladder. However, with injuries to the spine resulting in paralysis of the bladder, the conditions are quite different. The atonic condition of the vesical musculature will not, as a rule, cause sufficient renal back pressure to injure the kidneys or ureters. Furthermore, congestion and trauma to the bladder itself as the result of retention will not follow to the extent observed with intact vesical musculature. Overflow of the bladder usually will be established, and there is much less danger of ascending infection than would occur after catheterization. Recommendations that the bladder be allowed to overflow rather than that the catheter be used, have been previously suggested by a number of observers, including Plaggemeyer, Wesson, and Cabot.

Chronic retention of urine resulting from an atonic bladder seems to have quite different results, and produces a different cystographic picture (Figs. 2 and 3) than the chronic retention seen in most cases of obstructive retention. Instead of impairment of the ureterovesical protecting mechanism, and impairment of ureteral peristalsis, together with reflux of vesical content often as far as the renal pelvis, such as frequently occurs in the presence of obstruction, the quite different picture seen in the presence of vesical atony, is slowly increasing residual urine and vesical decompensation. Apparently the ureterovesical barrier, and ureteral peristalsis adjust themselves to the degree of impaired contractile power of the detrusor muscles, so that little or no ureteral reflux occurs. Only when ascending ureteritis has impaired the function of the lower part of the ureter will this result. It is surprising how often patients are observed who have had atony of the bladder of varying degrees for many years, without evidence in the urogram of reflux or of any impairment of the lower part of the ureter or of the kidneys.

Patients frequently are observed who have insidious, progressive urinary obstruction, and whose bladders are so distended that they reach the upper part of the abdomen. In one case, recently observed, the mass suggested a pancreatic cyst, but fortunately catheterization proved its nature and prevented abdominal exploration. Not only are such patients singularly free of fever and chills, which ordinarily accompany intermittent or acute prostatic obstruction, but as a general rule they give no evidence of retention of urea, are often unaware of any particular urinary difficulty, and if a catheter has not been passed prior to their admission, the urine will be found negative on microscopy. The lack of renal injury in such an instance can be attributed to decompensation taking place in the detrusor muscles rather than in the ureterovesical mechanism. At any rate, lack of hypertrophy of the vesical wall has protected the kidneys.

SUMMARY

Atony of the bladder is never primary. It is caused either by abnormal innervation, by obstruction, or by both factors. However, for the purpose of clinical differentiation, atony resulting from disease affecting the innervation may be regarded as primary. Continuous retention of urine from any cause will produce atony of the vesical wall. In some cases it may be difficult to determine which factor is involved. With most cases of atony, obstruction, either primary or secondary, is the predominating factor.

The factors involving sphincteric dysfunction are: (1) imbalance of innervation, with predominance of the sympathetic or filling nerves; (2) rigidity or failure of adequate relaxation of the internal sphincter referred to as dysectasia; and (3) apparent failure of co-ordination of reflexes involved in the act of micturition centering in the vesical neck, to which the term achalasia has been given. The first condition can be favorably influenced by presacral neurectomy and the second condition usually can be remedied by thorough transurethral resection. Knowledge concerning cases in which other causes are operative, is insufficient as a basis from which to determine treatment, but in one case of this type, presacral resection restored function to normal.

The abnormal tissue, which interferes with function of the vesical neck may in some cases be

easily overlooked. It is necessary to remove such tissues completely and to free every cicatricial contraction in order to restore sphincteric function. Sphincteric abnormality in the female presents problems quite different from those offered by corresponding conditions in the male. In most cases, judicious removal of sphincteric tissue will overcome retention, but subsequent presacral neurectomy may be necessary. Localized or partial atony may follow destruction of branches of the pelvic nerves in the course of a bladder operation. Various other types of atony may occur.

With acute retention such as often occurs following abdominal operation, the advisability of drainage of the bladder before it becomes overdistended should be emphasized. In contrast, with retention following extensive injury to the spine, overflow of the bladder should be permitted rather than catheterization.

It is evident that much still remains to be discovered in the mechanism of micturition and concerning the various lesions which may affect it.

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TRAUMATIC OSSIFYING PERIOSTITIS OF THE NEWBORN

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A NEW type of birth injury is herewith presented with illustrative cases, because it is a frequent possibility in the practice of every physician doing obstetrics. A review of the literature does not disclose any previously reported injuries similar to these. Due to the relatively late appearance of the X-ray diagnosis, this type of birth injury probably has been overlooked often. Consequently, the cause of pain, limitation of motion, swelling and discoloration of the injured part, which are the chief clinical findings, has been attributed to injury of soft tissues only. As the reported cases illustrate, recovery is spontaneous and the patient requires no special treatment other than the application of external heat and the prevention of contracture.

CAUSE OF INJURY

In studying this series, all of which were breech extractions, we have concluded that the injury is probably due to: (1) too strong traction on the extremity, (2) a twisting pull on the leg due to the inability on the part of the accoucheur to rotate the line of traction with the rotation of the fetus as it accommodates its large diameters to those of the birth canal, (3) the inability of the accoucheur to bring down both feet so that traction may be equally distributed, and (4) the too hasty attempt to complete the delivery. The injury to the humerus resulting because the arm was extended alongside the head calls attention to the danger of such delivery of the arms.

When version and extraction is chosen as the method of delivery, it is often done at a most unpropitious time, that is, after the membranes have ruptured and as a court of last resort. Strong traction then becomes necessary.

INTERESTING FEATURES

Several interesting features may be noted in this group of cases. Immediate X-ray examination is negative. The calcium deposit becomes visible only after 1 or 2 weeks. Recovery takes place spontaneously, in all the cases which we have observed. Recovery time seems to be in direct proportion to the extent of the injury—4 to 12 weeks in our series—and no permanent disability has resulted. Two cases were followed until they walked.

PATHOLOGY

A tearing or stripping of the periosteum of the femur or humerus occurs most often at its weak-

Fig. 1. Case 1. First examination, baby 40 days old. The left femur shows considerable elevation of periosteum in the upper part and slight elevation in upper and middle thirds of the shaft. The space between the periosteum and cortex at the upper extremity is filled with periosteal new bone formation.

Fig. 2. Case 1.¶ Second examination, baby 4 months old. The left femur shows considerable absorption of periosteal new bone shown in Figure 1.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3. Case 2. First examination, 3 days after birth. No evidence of fracture, dislocation, or pathological condition.

Fig. 4. Case 2. Second examination, baby 26 days old. The right femur shows considerable stripping of periosteum of entire circumference of shaft. The space between periosteum and cortex is filled with periosteal new bone formation.

Fig. 5. Case 2. Third examination, baby 4 months old. The right femur shows considerable absorption of periosteal new bone shown in Figure 4.

est point of attachment, the epiphysis, and the maximum strain of the traction is imposed upon the proximal epiphysis. If the trauma is more severe, we observe that the stripping follows down the shaft with further subperiosteal hemorrhage as in Case 2.

DIAGNOSIS

Diagnosis is important and difficult until one has followed through a case. Osteomyelitis and epiphysitis were both suggested on our first case. Fracture was the opinion of one roentgenologist. Sarcoma was also considered. In truth, the lesion is similar to myositis ossificans, which has its etiology in some instances, at least, in torn periosteum. A rapid proliferation of the periosteal osteophytes takes place with deposit of calcium. One must keep in mind that this X-ray visible periosteal injury is but part of the hemorrhage from muscle and fascial tearing.

Fig. 6. Case 3. First examination, baby 5 days old. The pelvis and femora show no evidence of fracture, dislocation, or pathological condition.

SUMMARY

1. A new type of birth injury connected with breech delivery is described.

2. Roentgenograms taken from 7 to 14 days after birth would show this to be a common injury from breech extraction.

3. Essential lesion shown in the roentgenograms

Fig. 7. Case 3. Second examination, baby 24 days old. Left femur shows considerable elevation of periosteum of upper extremity and slight elevation of upper and middle thirds of shaft. The space between periosteum and cortex at the upper extremity is filled with periosteal new bone formation.

is an ossifying periostitis about the proximal epiphysis.

4. Treatment is not specific and recovery is spontaneous without disability.

CONCLUSION

Too much traction on the legs or arms during breech delivery may cause extensive muscle and periosteal injuries resulting in ossifying areas.

CASE HISTORIES

All babies were born in the Hackensack Hospital, Hackensack, New Jersey; all were first babies; all breech deliveries.

1. Baby M., No. 31557. The child was born December 3, 1932; labor was prolonged—posterior position. Delivery was accomplished by podalic version and breech extraction. It was noted that "the child was delivered without injuries" but it did not breathe well. It was placed in a respirator for one-half hour. The child left the hospital in good condition. The trouble with its leg was first noticed about 6 weeks after birth. The right thigh was kept flexed. Motion was painful. An X-ray picture on January 12, 1933, showed the peculiar calcium deposit around the epiphysis of the neck of the right femur. The family was greatly disturbed. Two orthopedic men said that there was a fracture and that the leg should be put up in a cast. Another said that the condition was an inflammatory one and should be left alone. No treatment was given and the condition cleared up entirely. X-ray examination 3 months later (Fig. 2) showed that the proliferative process had entirely disappeared.

2. Baby S., No. 31870. The child was born December 26, 1932. The child was in frank breech position. Labor pains became ineffectual. It was necessary to grasp the foot to create traction. The head was caught on the perineum. Forceps were applied. The baby weighed 6 pounds, 15 ounces; it was 21 inches long and across shoulders 14½ inches; the head measured 15 inches. The second day it was noted that the right thigh was swollen, tender, and was held in abduction. X-ray film (Fig. 3) was taken on December 29, 1932, and was negative. It was noted that while baby moved right leg a little, it seemed as though it was partially paralyzed. Motion caused pain. The condition slowly improved without special treatment. An X-ray examination on January 24, 1933 (Fig. 4) showed large area of calcification in what must have been an extensive subperiosteal hemorrhage. After 3 months the leg was practically normal. X-ray film on February 29, 1933 (Fig. 5) showed much less subperiosteal deposit.

3. Baby A., No. 32549. The child was born February 25, 1932. It was in posterior position. The mother's pelvis was small. Delivery was very difficult and was accomplished by podalic version and breech extraction. The mother went into obstetrical shock from which she rallied slowly. The baby weighed 6 pounds 12 ounces; its length was 22½ inches, shoulder width 14 inches; the head 14 inches. The day after birth it was noted that the left leg and foot were edematous, discolored, and caused pain when moved. X-ray examination on March 2, 1932 (Fig. 6) showed no pathological condition. The baby remained in the hospital 4 weeks. The swelling and pain began to diminish after the first week and the child gradually used the leg more. An orthopedist on March 13, 1932 suggested that the condition was essentially a nerve injury. The leg improved but on discharge March 23, 1932, a roentgenogram (Fig. 7) showed the large amount of osseous formation about the upper epiphysis of the femur. Follow-up at home reports that the child recovered completely.

Fig. 8, left. Case 4. First examination, baby 9 days old. Left humerus shows moderate elevation of periosteum of external surface of upper extremity, with slight periosteal new bone formation.

Fig. 9. Case 4. Second examination, baby 14 days old. Left humerus shows moderate elevation of periosteum of external surface of upper extremity with moderate periosteal new bone formation.

4. Baby H., No. 35508. The child was born December 6, 1933, after a prolonged labor. It was in frank posterior position. Manipulation was difficult. Delivery was accomplished by podalic version and breech extraction. There was a third degree laceration and severe postpartum bleeding. The left arm was delivered in extension alongside of the face. There was an injury to the left shoulder and arm which was noticed immediately after birth. The arm was limp and there was some wrist drop, which was thought to be a nerve injury. The child weighed 8 pounds 14¾ ounces; was 22 inches in length, head measured 14 inches, and shoulders 17 inches. On the second and third days it was noted that motion of his shoulder was painful and that the area around the deltoid was slightly swollen and tender. A roentgenogram was taken on December 15, 1933 (Fig. 8) and showed an area of subperiosteal hemorrhage about the epiphysis of the upper extremity of the left humerus. A second X-ray film on December 20, 1933 showed more calcification of same area. During the period in the hospital the child's arm improved steadily. The wrist drop disappeared and motion and strength of the arm returned although there was a tendency to hold it in a typical Erb's palsy position. Since discharge baby has recovered complete function.

A CONSTRUCTIVE CRITICAL ANALYSIS OF MAXILLARY SINUS SURGERY

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THE surgical anatomy of any particular part of the human mechanism is the foundation upon which the success of a mechanical procedure depends. This statement is not intended to detract from the value of other known basic principles of medicine. The maxillary antrum, a cavity in the superior maxillary bone, varies in size and shape. It is the result of an invasion of the respiratory mucous membrane during life (4). Though modified it retains much of the basic character of the respiratory structure. If this presentation savors somewhat of the critical, its object is constructive, with an attempt to analyze the subject presented in a fair, just, and impartial manner. It deals with the applied surgical anatomy. The chemistry, physiology, pathology, and bacteriology will be mentioned only as correlating influences.

Drainage in the presence of exudative purulent infection is a surgical axiom. It is especially referable to acute infection. Its application is at times modified by chronicity, in that tissue resources have in a measure fulfilled the necessary need. This is not an uncommon clinical observation. The non-surgical treatment of empyema of the antrum has been advised (10).

The trend of maxillary sinus surgery during the past 2 decades has been to the so called radical method. A better description would have been one using the term complete. It has been manifested by the usual concomitant enthusiasm, many times far beyond its real merit and value. In this the writer assumes his full share of responsibility (16). Though much has been published on the surgery of the maxillary sinus, the greater portion of these observations have been referable to the histopathology of the mucous membrane. Little has been presented on the surgical anatomy. Whether the trend to rely upon the X-ray has been a factor the writer is unable to state. It would seem that the surgical anatomy of this structure is a closed book and that little new may be added by investigating this particular aspect of the subject. From a series of observations, the writer has assumed a somewhat different attitude than he formerly held.

In this presentation, two principles involved in radical maxillary sinus surgery are discussed. They are: first, the histological fact that the mucous membrane of this structure normally possesses cilia sweeping its contents toward the natural ostium, that this ciliary activity varies from that of a kinetic action to one of inaction with a potential reserve, depending upon the degree and type of pathology present; second, a series of anatomical observations and their surgical application. Beyond the realm of these two principles, this presentation is not concerned. It is assumed that a final clinical result is the object sought in any method of therapy. Changes in the mucosa, the presence of foci, their relation to systemic invasion and disturbances must be weighed in the final analysis of clinical observation.

Ciliary activity of the respiratory mucous membranes has been studied by innumerable observers. McDonald and his co-workers draw certain conclusions, one of which is that "by way of anticipation their work points directly to the existence of neural, chemical, and physical control mechanism for regulation of the rate of ciliary activity in higher vertebrates." Their observations are the result of much animal and pharmacological experimentation. They quote freely from the opinion of others. Bloomfield states: "In a study of the etiology of respiratory infections, we have in the past overemphasized secondary factors, such as identification of the offending organisms and the determination of its mode of transposition to the human host, but have neglected the most essential factor, namely the respiratory surface itself. It is only when some abnormal change or injury occurs in the host, that colonization and invasion occurs." Our ciliated surfaces do not become infected whenever pathogenic micro-organisms gain access to them. This is a matter of common observation. It has been demonstrated experimentally, that when many types of pathogenic bacteria are brought into contact in large numbers with the upper respiratory mucous membrane of healthy persons, these microorganisms are easily disposed of within a very short time without colonization and invasion (1,5) These principles apply to other structures of the body as well. I refer to the gastro-intestinal tract, fallopian tubes, and male urethra.

Small gross sections of mucous membranes removed from infected antra, both acute and chronic when placed upon a warm microscopic stage, clearly demonstrate ciliary activity. The writer

[1]Deceased

Fig. 1. Frontal section through both superior maxillæ in the plane of the anterior one-third of the inferior turbinate. It shows at *A* and *A'* the maxillary sinus and floor, *B* and *B'* the inferior turbinate, *C* and *C'* the nasal floor, *D* the nasal septum, *E* and *E'* the inferior conchal crest. Notice the difference in the corresponding levels of the nasal and maxillary sinus floors.

has made such observations, and has seen it demonstrated in the laboratory of the Massachusetts Eye and Ear Infirmary under the direction of Dr. Harris P. Mosher. This ciliary activity varies. It may be sluggish, nevertheless it is usually present. Proetz states: "The fact that normal ciliary activity persists in the presence of even the worst sinus infections demands a new conception of the mechanism of bacterial penetration in these parts." It is the writer's opinion that these observations are of great importance in the application of any surgical procedure referable to the maxillary sinus. McDonald's findings based upon experimental study seem to prove that ciliary activity depends to a great degree upon a neurogenic control, and that any excess moisture modifies the extent and direction of ciliary propulsion. Assuming these observations to be true, it is evident that a fundamental principle in the treatment of this cavity would be the conservation of the cilia, regardless of their activity, by the most logical method based upon the surgical anatomy of the part involved. By so doing a physiological process is conserved and a surgical principle maintained. The virtue of the complete ablation of the mucous membrane and the clinical result must be defended against these facts.

The surgical anatomy of the maxillary antrum varies (8). Textbooks describe its embryology, configuration, and relation to surrounding structures. To correlate the applied anatomy relative to the surgery of this structure a series of maxillary bones were sectioned and observations made in reference to the comparative position of the most dependent part of the antral cavity, with that of the floor of the nasal fossa. Two sections, one through the anterior third and the second through the posterior third of the inferior turbinate bone in the frontal plane, were made on a series of 64 superior maxillary bones. In 4 others, sagittal sections were made through the antrum so as to obtain a mental picture of the general appearance of the floor and for the purposes of illustration. A total of 68 maxillary antra were sectioned and observations made upon 196 specific sections. The results are presented not in reference to the sum total of sections but to the maxillary sinus floor as an entity and comparatively with the floor of the nasal fossa. The object sought was to determine in what percentage of antra drainage might be expected from the aspect of mechanical dependency. Other observations made in the respective antra were noted, principally for personal enlightenment, and, though not referable to the subject presented, have been briefly mentioned and reported.

A brief discussion of the nasal floor and the lateral nasal wall in reference to the maxillary antrum is necessary to clarify the findings. Anatomists describe the inferior turbinate as articulating with the inferior conchal crest on the medial surface of the body of the maxilla. Below the crest is a smooth concave surface belonging to the inferior meatus of the nose. The floor of the sinus descends below the level of the floor of the nasal cavity. From the floor of the antrum in the majority of cases septa of varying dimensions project upward and divide the cavity. The most frequent separates the premolar region in front from the third molar region behind, and may divide the sinus into two chambers (3, 9). Arthur Logan Turner, from a series of observations concludes that, in a maxillary sinus of average dimensions, the floor is on the plane of the floor of the nasal fossa. This statement raises the interesting

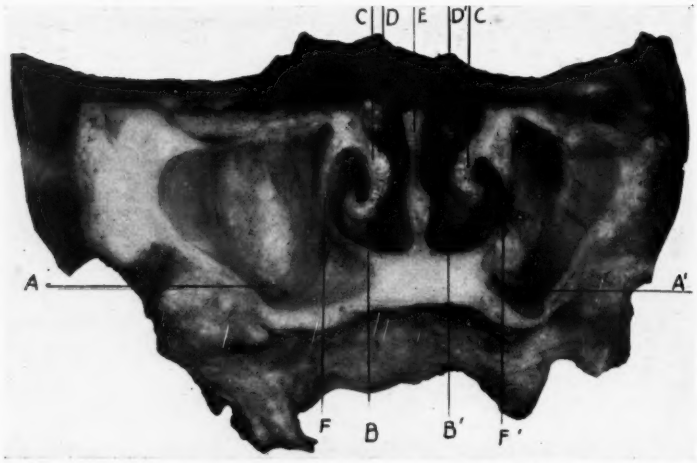

Fig. 2. Frontal section through both superior maxillæ in the plane of the anterior one-third of the inferior turbinate bones. It shows at *A* and *A'* the maxillary sinuses and floor, *B* and *B'* the nasal floor, *C* and *C'* the inferior turbinate bones, *D* and *D'* the middle turbinate bones, *E* the nasal septum, *F* and *F'* the inferior nasal conchal crest. Notice the difference in the corresponding levels of the nasal floor with that of the maxillary sinus floor.

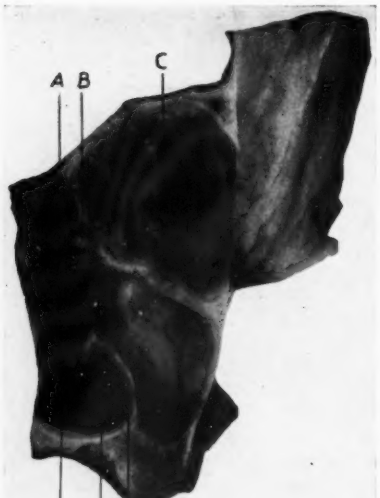

Fig. 3. Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. *A* the middle turbinate, *B* the ethmoid labyrinth, *C* the orbit and contents, note dark shadows of eye muscles, *D* the nasal floor, *E* the inferior turbinate bone, *X* the inferior conchal crest, *F* the maxillary antrum and floor. Note that in this specimen the floor of the maxillary sinus is on the level of the floor of the nasal sinus, but also note the thickness of bone of the lower part of the conchal crest.

Fig. 4. Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. *A* the orbit and contents, *B* the maxillary floor and sinus cavity, *C* the posterior part of the frontal sinus extending over the orbit, *D* middle turbinate bone, *E* probe in natural ostium of maxillary sinus, *F* the inferior turbinate bone, *H* the nasal fossa and floor, *X* the inferior conchal crest. Note the thickness of bone between the floor of the nasal fossa and the floor of the maxillary sinus.

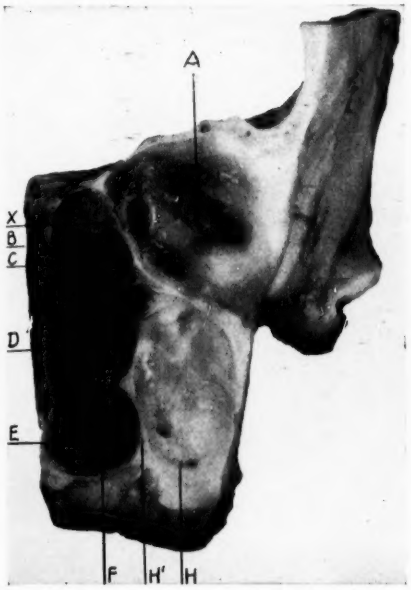

Fig. 5. Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. *A* the orbit and contents, *B* the nasal septum, *C* the superior turbinate bone, *X* the ethmoid labyrinth, *D* the middle turbinate bone, *E* the inferior turbinate, *F* the nasal floor, *H* the floor of the maxillary sinus, *H'* the inferior conchal crest. Note in this specimen as in Figures 3 and 4 the thickness of bone between the floor of the maxillary sinus and the nasal floor. Also notice dark areas in orbital contents representing internal rectus and inferior oblique muscle.

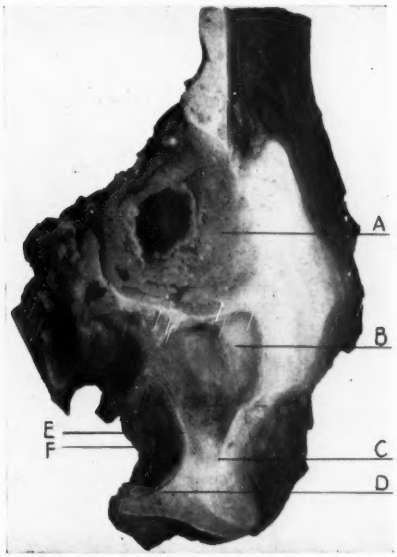

Fig. 6. Photograph of section which shows the floor of the maxilla to be above the floor of the nasal fossa. *A* the orbit and contents, *B* the maxillary sinus with its floor on the level of the inferior turbinate bone *F*, *C* the floor of the maxillary sinus, *D* the nasal floor, *F* the conchal crest. It demonstrates with what ease drainage may be obtained in such a case via the inferior meatus in contradistinction to that shown in the other photographs.

problem of how often does a maxillary sinus of average dimensions occur, and in what percentage of antra does it, or does it not apply? Neivert reports certain phases of several hundred dissections from the Daniel Baugh Institute of Anatomy. He explains the presence of septa and abnormal ostia by stating that the embryology is an outpouching from the primitive ethmoidal infundibulum, and therefore we cannot expect to find the ostium maxillæ to be of definite size and location. I have found this to be true.

In so far as the practical applicability of drainage into the nose from the maxillary sinus is concerned, it is the writer's opinion that the inferior conchal crest is the structure which serves as a barrier in attaining this end. This crest is compact bone, thick in its lower part, and rises above the nasal floor at times as much as 10 millimeters. It is doubtful whether it is possible in many cases to remove the crest to the level of the nasal floor without undue trauma. The use of the Halle burr has been advocated (15). The writer has observed Halle's technique as he operated and has personally used it. There is no question but what one is able to remove more of the crest by this method. Whether the added trauma by the use of the burr compensates for the added drainage obtained must be questioned. The surgical anatomy presented does not warrant its use, other than in a limited number of cases. It possesses great merit in trimming roughened edges and completing a neat surgical procedure in the nasomaxillary approach as advocated independently by Canfield and Sturmann.

Of the 64 maxillary antra sectioned in a frontal plane, the following facts were determined: in 19 it was clearly demonstrated that some part of the antral floor was below the most inferior plane of the nasal floor, in 21 the most dependent part was on the plane of the nasal floor; in 14 it was on the plane of the osseous conchal crest varying from the base to upper border; and in but 10 of the specimens was the floor of the maxillary sinus above the osseous conchal crest. In addition 17 of the antra were partially divided by septa, none

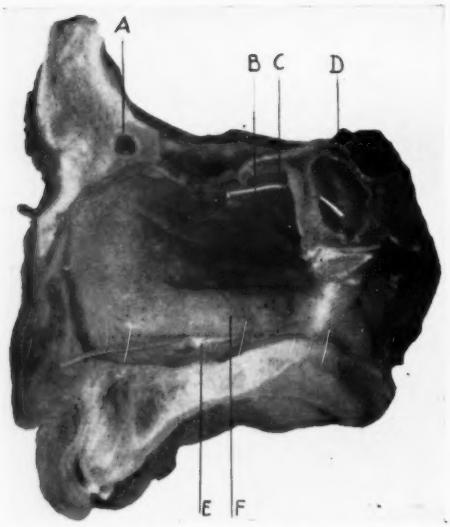

Fig. 7. Photograph of a saggital section through the nose. It shows at *A* part of frontal sinus, *B* the middle turbinate, *C* probe in sphenoidal ostium, *D* sphenoid sinus, *E* probe in artificial opening beneath inferior turbinate, shown at *F*. Notice difference between level of nasal floor and artificial opening. This opening was made with a chisel and instruments and with so severe trauma that it would be contra-indicated in an operative case. Biting forceps were also used to get the opening as low as possible.

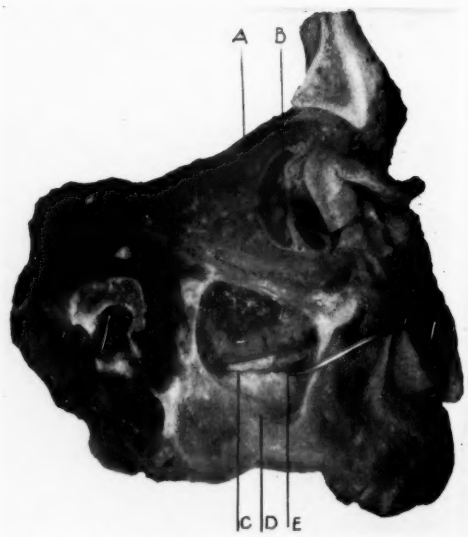

Fig. 8. Photograph of a saggital section through a right maxillary sinus. It is the same specimen as is represented in Figure 7. It shows the right maxillary sinus opened in the saggital plane. *A* the retrobulbar contents, *B* the eye, *C* the artificial opening in the inferior meatus, *D* floor of the sinus, *E* probe through artificial opening. Notice the amount of sinus cavity between artificial opening and floor of sinus, and how it would serve as a reservoir for secretion provided no added aid to drainage was had, such as presented in the text.

in their entirety. Nine showed more than one ostia, in 4 of which one of them communicated with the superior meatus. Seven demonstrated tooth root extension into the cavity (14). This observation was based upon 43 specimens, the others having had a dental extraction prior to, or during a previous head and neck dissection (Figs. 1 to 8).

Table I is a compiled tabulated report of the comparative observations made, referable to the floor of the maxillary antra, the nasal floor, and the osseous conchal crest.

In Table II is a summary of other observations.

Assuming that the observations as presented, referable to the surgical anatomy of the maxillary sinus cavity are true, what conclusions and deductions may be drawn? They are, that in 30 per cent of the observations dependent drainage without other aids is mechanically impossible. In 32 per cent, its attainment was highly improbable even by the use of the most drastic methods. In 22 per cent such drainage might be possible if drastic measures such as the removal of a great portion of the conchal crest be carried out. In but 16 per cent of the observations was mechanical drainage possible without added factors. In a composite analysis of the findings as presented, it was clearly demonstrated that in 62 per cent mechanical drainage, viewed from the aspect of dependency could not be expected without additional aid, and it was doubtful in another 22 per cent. These observations impress one with the necessity of some added force to accomplish

TABLE I

Frontal section	No.	Sagittal section	Total	Per cent
Below nasal floor	19	2	21	30 plus
Plane of nasal floor	21	1	22	32 plus
Plane of crest	14	1	15	22 plus
Above crest	10	0	10	16 minus
Total	64	4	68	

TABLE II

	No.	Per cent
Number of antra investigated	68	
Abnormal findings		
a. Partially divided by septa	17	25
b. Totally divided by septa	0	0
c. Multiple ostia	9	13
d. Ostia in superior meatus	4	6
e. Tooth roots in antra (based upon 43 observations)	7	16

drainage in a great per cent of maxillary antra treated by surgical procedure. It would appear that this added aid to drainage would be by conserving the mucous membrane when judgment so warrants. A large inferior meatal opening, provided it remains patent, attains the purpose of dependent drainage. Unfortunately, reliable inspection of the cavity cannot be accomplished by this method. Therefore, the utilization of a method where drainage is obtained with the added advantage of visual inspection of the cavity would seem the ideal to accept. In view of the difficulty caused by the frequent closure of an inferior meatal opening, and the variance of the pathology encountered, the writer believes that a nasomaxillary angle approach meets all the demands, from the viewpoint of the surgical anatomy as presented and the ciliary activity as reported in the literature. Such approach remains patent, the antrum may be visualized, and drainage is satisfactory. Superficial curettage of the mucous membrane has been advocated and is practiced by many. Even though condemned, the writer is an advocate of such procedure. Superficial pathology is removed, the cilia reform, and the neurogenic, hormonal, and physical potentiality of the membrane is not destroyed.

Since dogmatism has little place in medicine, any definite method of mechanical procedure that may be advocated must depend upon the basic principles involved. When they are found to be inapplicable to a particular method of therapy, the method must be altered to suit the principles. The nasomaxillary approach is not recommended as a universal procedure where surgery of the maxillary sinus is indicated. It is advocated as the method of choice in the majority of maxillary sinuses that may come to surgery. This opinion is based upon the principles of surgical anatomy and ciliary function. This treatise in no way detracts from that type of case in which the sublabial approach meets the need, nor does it belittle the ultraconservative inferior meatal opening when judgment so warrants its use. Clinical results must be analyzed from the benefits referable to the entire human organism and not only the antrum *per se*. This applies to its surgical application directly, or as an adjunct in the treatment of local or systemic manifestations as demonstrated in that great group classified in the category of allergy.

CONCLUSIONS

1. From experimental observations the cilia of the maxillary antral mucosa are probably controlled by neural, chemical, and physical forces.
2. Microscopic study showed infected antral mucosa to possess cilia in varying degrees of activity.
3. A study of the surgical anatomy of a series of maxillary sinus cavities indicate that dependent drainage is impossible in a great percentage of cases without some added aid.
4. It would appear that conservation of the mucosa with its cilia, even though inert, would be the logical force to conserve.
5. In a large percentage of cases, a properly constructed intranasal window should suffice. Its weakness is that it does not permit inspection of the cavity, and frequently fails to remain patent.
6. A nasomaxillary opening remains patent, is based upon the surgical anatomy of the majority of maxillary sinus cavities, and takes into consideration the ciliary physiology.
7. Mucous membrane ablation, as any method used, must be defended against such observations.
8. Results must be analyzed in the crucible of clinical medicine and surgery.

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TRIGEMINAL NEURALGIA

Experiences with, and Treatment Employed in 468 Patients during the Past 10 Years[1]

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ALTHOUGH knowledge of the present day methods used for the alleviation of trigeminal neuralgia is widespread, there are, nevertheless, so many conflicting views relating to different aspects of treatment in the minds of both patients and physicians that it has seemed worth while to review our experiences in dealing with a fairly large group of individuals suffering from this malady, and in so doing to relate what our policy has been in recommending various types of medical and surgical therapy.

It is still a frequent occurrence to have intelligent patients throw up their hands in horror when the so called radical operation of sensory root resection is proposed. Many of them say that they have been told, either by friends or physicians, that this operation should be undertaken only "as a last resort," not only because they have heard that it was extremely dangerous, but because those who underwent this procedure were almost certain to be left with a "drooping face." It seems almost incredible that either or both of these highly overdrawn statements should persist today in view of their frequent refutation in medical literature by surgeons who have had the widest experience with trigeminal neuralgia. It cannot be denied that there is always some degree of danger in any surgical undertaking, but the mortality in operations for partial or total section of the sensory trigeminal root is, or should be, less than 1 per cent when the procedure is carried out by those who have been thoroughly trained in neurosurgery.

In regard to the facial palsy which is, apparently, so often associated in the lay mind with the radical operation, it must be said in all fairness that this does occasionally occur, although its incidence is certainly not greater than 5 per cent. Furthermore, it is seldom complete, and in the vast majority of patients clears up promptly and completely within 1 or 2 weeks. In rare instances it may take longer, but in our own series there has not been a single case in which paralysis has been permanent.

In contrast to what has just been observed concerning division of the trigeminal root, one hears from perhaps an equal number of patients that alcohol injections are either of no value or that they are so painful they would rather have their neuralgia than an injection. Again, in our opinion, these statements are not only greatly exaggerated but based upon faulty understanding. Alcohol injections, especially of the two lower divisions of the trigeminal nerve always give many months' relief from pain, *provided the nerve trunk has been injected.* If they do not give such relief, it means either one of two things: namely, that the nerve was not injected or the patient had some other type of neuralgia. As to the pain of giving an alcohol injection, the following, we think, is a fair statement. Most authorities believe that these injections should be given either without an anesthetic or after a preliminary injection of novocain around the nerve, because if the patient is under general anesthesia there can be no co-operation as to when the nerve is reached and the percentage of successful injections is consequently greatly lessened. This means that a certain amount of pain must be endured, but we have found that by using a small bore needle (22 gauge) there is in the great majority of cases only a prick when the needle pierces the skin, and subsequently a sharp but usually momentary radiating pain when the needle point enters the nerve. The latter is almost exactly like the pain which the patient has experienced frequently in the course of his neuralgia and is dissipated within a few moments by the immediate injection of alcohol which contains a little novocain.

From the foregoing observations it must be evident why no hard and fast rule can be laid down as to when injection or operation should be advocated. Indeed, there are some patients in whom the affliction is fortunately so mild that they may require no treatment at all or may perhaps be benefited by inhalations of trichlorethylene. We will return later to a fuller discussion of these subjects.

DIFFERENTIAL DIAGNOSIS OF TRIGEMINAL NEURALGIA

In order to institute proper treatment for the condition in question, as in any other malady, one must be certain that the patient has true trigeminal neuralgia and not one or another of the atypical neuralgias or pains in the facial region which at times may simulate tic douloureux. Sev-

[1] In addition to the patients seen and treated at the Lahey Clinic since November, 1932, this group represents all patients in the senior author's personal series at the Peter Bent Brigham Hospital since 1925. During the period mentioned at the Brigham, Dr. Harvey Cushing most kindly referred to the senior author for treatment practically all cases of trigeminal neuralgia, whether private or public ward patients. This note is a grateful acknowledgement to Dr. Cushing as well as an explanation of the series.

eral of these atypical neuralgias were described in detail by Cushing (1), in 1920. Although the diagnosis may be made almost at a glance when a typical paroxysm is observed, it is not always an easy matter; therefore, a few differential points concerning some of the commoner conditions causing confusion may be helpful.

Dental infections are common and small cavities with foreign objects, such as bristles of a tooth brush may cause pain which simulates a minor trigeminal neuralgia. Sinusitis can be ruled out by local tenderness and X-ray. Facial injuries usually have the history of trauma and are thus not readily mistaken, although one patient in the present series had a recurrence of pain for several weeks in his right lower jaw every time he ate or talked, 9 years subsequent to a total sensory root avulsion on the same side. Examination showed a complete anesthesia of the right trigeminal region and a definite localized tenderness over the angle of the right mandible. X-rays disclosed a fracture of the right lower jaw at the angle. There was no history of trauma with the exception of the fact that the patient had eaten some hardtack the night before the pain started. Transmission of pain in this instance must have been through sympathetic fibers.

Postherpetic neuralgia involving the trigeminal nerve usually clears up in several weeks in young individuals but in adults it may last for months or years with remissions. The pains are limited to the branches involved and are more or less continuous. However, they may come on spasmodically. The etiology of such a neuralgia is implied by the history, and examination usually shows the scars of herpetic vesicles together with hyperesthesia of the skin. The diagnosis is important because the pain is seldom if ever controlled by alcohol injection or even posterior root resection.

Sphenopalatine or Sluder's neuralgia caused by some infectious process of the sphenopalatine ganglion is probably relatively uncommon. The pains are usually at the base of the nose, around the upper jaw and eye, radiating backward to the ear and mastoid region, extending at times to the back of the neck, shoulder, and upper extremity. Neuralgias attributed to the geniculate ganglion involve the sensory portion of the seventh cranial nerve causing severe otalgia. The pain of glossopharyngeal neuralgia involves the tonsils, pharynx, and posterior part of the tongue. It is the same type of pain as trigeminal neuralgia, but differs in its distribution.

Sympathetic pains are usually described as dull, aching, burning, or pressure pains varying in intensity. They seldom follow any anatomical distribution of nerves. The orbit, cheek, and temporal region are usually involved. The pains usually last several hours, and may persist intermittently for months. The intensity usually varies with the nervous stress of the patient. Associated symptoms such as flushing of the face, increased lacrimation, and salivation are common.

Tumors involving the gasserian ganglion produce severe and usually persistent pain while examination reveals the relative hypesthesia and later a sensory and motor paralysis. High cervical spinal cord tumors have been alleged to cause severe pain in the trigeminal region, but in these cases there are other associated signs and symptoms, making the diagnosis possible if a careful general neurological examination is made.

SYMPTOMATOLOGY

The subjective symptoms of trigeminal neuralgia are usually so graphic that the diagnosis is unmistakable. A frequent story is that the patient was seized with a sudden pain in one side of the face "like a bolt of lightning," lasting for several moments, leaving as suddenly as it came, with no residual aches or pains and reappearing at frequent intervals. The character of the pains are detailed by different adjectives depending on the descriptive powers of the patient and the severity of the attacks, but all with the same meaning. The pains come on in paroxysms of rapid, successive stabs confined to the limits of the branch or branches involved. Some authors state that pains should always radiate to the very end of the branches at the median line. In our patients, when paroxysms were severe, pain has extended to the peripheral limits of the nerve but in milder attacks this has not been the rule. Too much emphasis cannot be laid upon the fact that there is practically always entire freedom from pain or discomfort between attacks. There are frequently periods of remission during which time the patient is wholly relieved, or is fairly comfortable for a matter of several days, months, or even years. During a severe bout of pain, the paroxysms vary in frequency, coming on every few minutes or only a few times daily. A region of increased irritability commonly called the "trigger zone" is often present and when stimulated by washing the face, shaving, chewing, talking, or smiling, a spasm is induced, thus explaining the masklike expression of the affected side of the face, also the accumulation of dirt as well as the peculiar headgear some patients use as a prophylactic. Other objective signs than those mentioned vary with the individual. Patients with a

highly nervous makeup may demonstrate their agony during an attack by throwing themselves on the floor, screaming, and rubbing the face on the affected side. Others more stoical may merely rub their cheek or make a few chewing movements, stopping any conversation they are engaged in until the pain has left, and then resume their conversation.

ETIOLOGY

The cause of trigeminal neuralgia is unknown. The most plausible theory would seem to be that of Sir Wilfred Harris (6), who believes that dental infections are in all probability the underlying factor, although it is well recognized that once the neuralgia has started, removal of infected teeth has no influence upon it. Dandy feels that external pressure upon the sensory root by tumors or blood vessels may at times be the cause of tic douloureux. Multiple sclerosis has also been given as a possible etiological factor, but only 3 cases of this malady have been found in our series. Trigeminal neuralgia occurs most frequently in patients of middle or advanced age. In our group, 60 per cent occurred between the ages of 50 and 70 years and over 90 per cent in patients between 40 to 80 years of age. The youngest patient was 16 and the oldest 93 when they came for treatment.

TABLE I.—AGE INCIDENCE

Age in years	Cases
10–20	1
20–30	11
30–40	29
40–50	46
50–60	114
60–70	157
70–80	80
80–90	9
90–100	1

Women were affected much more frequently than men in our series in the ratio of almost exactly 60 to 40 per cent. Fifty per cent occurred on the right side, 45.3 per cent on the left, and 4.1 per cent were bilateral.

TABLE II.—SEX INCIDENCE AND SIDE AFFECTED

	Cases	Per cent
Males	186	40.8
Females	282	59.2
Right side	237	51.7
Left side	202	44.2
Bilateral	19	4.1

The division involved alone most frequently was the third, which occurred in 42.1 per cent of all cases; the second division in 24 per cent; the second and third together in 21.9 per cent; the first and second together in 3.8 per cent (Table III).

TABLE III.—FREQUENCY OF DIVISIONS INVOLVED

Division of trigeminal	Per cent
1st division	2.0
2d division	24.3
3d division	42.3
1st, 2d, 3d divisions	4.7
2d, 3d divisions	21.9
1st, 2d divisions	3.8

TREATMENT

We feel that to the present day there is no ideally perfect treatment for trigeminal neuralgia because although permanent relief of pain can be promised the patient, there are certain discomforts associated with the numbness which must be substituted for this. In explanation of such a statement, however, it must be said at once that certainly 90 per cent of all persons who are now treated by modern methods would consider the treatment as most satisfactory and not regard the discomfort from numbness or paresthesias as any particular hardship. Even during the past decade, many things have been learned which make the treatment more comfortable and lessen the possibility of operative or postoperative complications. Preserving the motor root (5) and conservation of the ophthalmic fibers (4) in the lower division neuralgias are striking examples directed toward this end. Furthermore, the total or differential injection of the ganglion as practiced by Harris (7) has great possibilities in skilled hands. Finally, the operation advocated by Dandy, in which the nerve root is partially divided at the pons, has apparently reduced the resultant numbness to a very great extent, but we believe that this procedure is at least potentially more dangerous than the accepted temporal route.

The treatment of trigeminal neuralgia may be divided into the conservative and radical, the conservative consisting in non-operative and minor operative procedures, the radical in root avulsion. As already intimated, in order to obtain permanent relief, one must exchange pain for a permanent numbness of the part involved. Such an exchange is accepted cheerfully by the majority of patients who grasp at anything which will end the excruciating pain. However, it must be emphasized that a few mind the numbness and paresthesia following avulsion more than the previous pain, and it is because of this small group that one hesitates to advise the radical operation before acquainting them thoroughly with the numbness by less radical measures.

Therefore, as with any other disease, the treatment must be suited to the patient and not the patient to the treatment.

We do not advocate any single procedure, but wish to describe our own method of dealing with individuals having trigeminal neuralgia. Patients usually consult a neurosurgeon after every possible medical treatment has been tried. The teeth, as a rule, have been removed on the side affected, although in recent years this has been less frequent since dentists recognize the malady and advise against this practice, if the X-ray shows no pathological condition. Narcotics are frequently taken, but fortunately do little to relieve the pain, thus preventing drug addiction. When the patient does come he is interested usually in getting rid of the pain immediately.

Treatment with trichlorethylene. If there is no question as to the diagnosis and the attack is mild, inhalations of trichlorethylene are advised with definite instructions that 20 to 30 drops be placed on a handkerchief or piece of cloth and held closely to the nose. The fumes are to be inhaled until no odor is detected, a matter of a few minutes. This is to be done three times a day for two weeks, regardless of whether the pains are present or not, provided pain is not so intense that the patient should be in a recumbent position on one side or the other so that if they should become partly anesthetized, the hand will drop away from the nose, stopping the inhalation.

Ninety patients were given treatment with trichlorethylene and have been followed carefully. In this group, nearly one-half obtained sufficient relief so that they did not feel it necessary to have any other form of treatment for their neuralgia for periods of 6 months up to 6 years. The remaining patients obtained no relief or it was so slight that something more radical was indicated within a short space of time.

Alcohol injections. If no relief is obtained from trichlorethylene, the patient is then asked to come in for alcohol injection of the peripheral nerve trunk. At no time is avulsion of the root advised without first giving at least one such injection. This policy is followed for two reasons: In the first place, it makes the patient acquainted with the numbness which must follow any surgical procedure upon the trigeminal system. This may seem to be a small matter, but experience has shown that some patients are greatly annoyed by such an anesthesia and the various sensations which accompany it. These sensations are described as "burning," "twisting," or "like wires in my face," and occasionally are complained of as much as or even more than the original pain. When an alcohol injection only has been performed, normal sensation returns to the area injected and later, when there is a recurrence of the neuralgia the patient is much more likely to be satisfied with treatment, realizing that after all, the discomfort from these paresthesias is not to be compared with the agonizing neuralgia pain. A second reason for preceding root section by an injection is to make sure, in the occasional instances in which the diagnosis may be uncertain, that the patient has true trigeminal neuralgia, since it is now well known that division of the sensory root of the trigeminal will not relieve the atypical facial pains which simulate tic douloureux. Both of these points as well as others were emphasized by Cushing (2) in 1920.

An alcohol injection can be performed quickly in the office with immediate relief of the pain in all cases, if a fair hit of the nerve has been made. At times, if two divisions are involved, mainly the second and the third, each is injected at the same session. Usually, however, the affliction has started in one branch only but pain may "overflow" into the area adjacent. In such cases, if an injection is made into the nerve primarily affected, this "overflow" is practically always controlled.

Before alcohol injections are attempted, one must have a thorough knowledge of the skull with relation to the structures around the exits of the nerve trunks. This can be obtained only by dissection of the head and neck, as well as by injecting the nerve trunks in cadavers with colored solutions, in this way becoming familiar with the bony landmarks and approximate depth of the foramina rotundum and ovale. After one has become acquainted with these landmarks on the cadaver, it is important, if possible, to see injections performed by someone who has had experience with the procedure and likewise to do injections on patients under supervision. A most important faculty to develop is that of being able to visualize deep structures in three dimensions.

For the actual injection a small instrument set is all that is necessary. This consists in a 5 cubic centimeter Luer-Lok syringe, two No. 22 gauge needles 3 inches long, a fine short needle for supraorbital and infraorbital injections, a centimeter measure, a hemostat, a prepared solution of 80 per cent alcohol containing 1 per cent of novocain, and a little bone wax to use as a marker on the needle. For all injections the patient is asked to lie flat on the back on a table of sufficient height for the operator to be in an easy position. For deep injections of the second and third divisions, the patient's head is turned well over to the oppo-

Fig. 1. Front view to show approximate upward angle of needle for third division injection.

Fig. 2. Posterior view showing relation of needle to auditory meatus in third division injection.

site side and rests on a sand bag about 2 to 3 inches in thickness. No premedication is given unless patients are unusually apprehensive and nervous. The reason for this is that the ultimate success of the injection depends on their co-operation.

It is not necessary for the operator to clean up or to use rubber gloves for giving injections in the manner to which we have become accustomed. Our preparatory routine is as follows: The sterile injection set is opened and with the sterile hemostat contained in the set an appropriate needle is adjusted to the syringe. If an injection at the foramen ovale or rotundum is contemplated, a bit of bone wax is pinched around the needle, 1 centimeter beyond the usual depth at which these structures are reached. Two cubic centimeters of the 80 per cent alcohol mixture is drawn into the syringe, after which the appropriate area on the patient's cheek is sterilized with 70 per cent alcohol. A small piece of gauze dampened with alcohol is placed over the area to be injected in order that landmarks may be palpated through this. The approaches which we use to the foramen ovale and foramen rotundum are essentially the same as those described by Hartel and Harris.

Third division injection. For this procedure the bone wax marker should be placed on the needle at a distance of 5.5 centimeters from the point, thus giving 1 centimeter leeway between this marker and the depth at which the nerve should be reached. The syringe with attached needle is taken in one hand, while the index finger of the other palpates through the sterile gauze the highest point of the notch in the lower border of the zygomatic process. The patient is then instructed concerning the procedure by being told that there will first be a slight prick as the skin is pierced, after which no great discomfort will be felt until the nerve is entered, when there should be experienced a pain similar to the neuralgic pain which ordinarily radiates down the lower jaw to the chin or to the front of the tongue. Patients are told particularly to let the operator know if pain radiates upward into the temple or backward toward the ear, because when radiation occurs in these directions it means that the needle has impinged upon the meningeal artery or the eustachian tube, respectively.

The sterile gauze is now removed from the cheek and the needle inserted just below the zygomatic notch at the point where a slight imprint will have been left by the palpating finger pressed upon the gauze. The needle is directed slightly upward and backward and at a depth of 4.5 centimeters, the nerve trunk may be reached upon the first attempt (Figs. 1 and 2). If pain radiates correctly, a drop or two of alcohol is injected. This causes a momentary severe pain over the course of the nerve, but is followed immediately by numbness and cessation of pain. If the nerve is not reached at the usual depth, our practice is to withdraw the needle a centimeter or two and then direct it somewhat forward so as

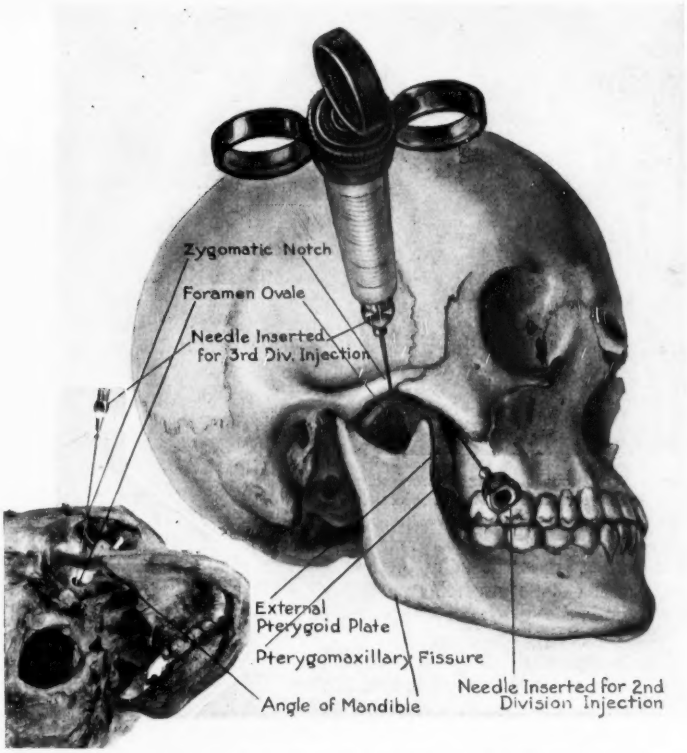

Fig. 3. Two views of skull to show various landmarks and relationships with needles inserted for second and third division injections.

to come down upon the external pterygoid plate. This is an essential landmark because the foramen ovale lies just posterior and slightly medial to it (Fig. 3). With this orientation the needle is again withdrawn somewhat and directed a little backward until the nerve is entered as evidenced by pain radiation. It may be necessary to repeat this process several times, and also it must be remembered that there are slight variations as to the depth at which the foramen lies. In some individuals it may be reached at slightly less than 4.5 centimeters, and rarely at a depth as great as 5 centimeters from the skin.

When the nerve trunk has been entered and a few drops of alcohol injected, the patient's lower lip near the median line is tested for anesthesia. This should be done with a pinpoint and the patient's eyes should be closed. If a fair hit has been made, the sensory loss is almost immediate on this portion of the lip, the lower gum, and half of the anterior two-thirds of the tongue. Having determined this, we then inject about 1 cubic centimeter of alcohol very slowly, often pushing the needle gently inward for a millimeter or two during the process in order to be sure that the substance of the nerve is wholly injected. The needle is then withdrawn and pressure made over its point of entrance with sterile gauze in order to prevent oozing. The patient is now asked to open the mouth. If injection of the third division has been complete, the lower jaw will deviate distinctly toward the affected side.

One further point regarding the injection should be noted. At times when the needle is in the proper position and depth, there is no radiation of pain down the jaw but severe pain is present at the tip of the needle. This happens in a fairly large percentage of cases. A drop of alcohol may then be injected and it usually brings on the radiation of pain followed by numbness, indicating that a fair hit has been made. The reason care should be taken in injecting only very small

Fig. 4. Front view of patient showing approximate position and angle of needle for second division injection from anterior approach.

amounts slowly is that at times the point of the needle enters the foramen ovale unwittingly. If the point happens to be in the subarachnoid space around the ganglion and alcohol is injected, severe reactions as well as permanent damage may be done. If, on the other hand, only a drop has been injected and the patient develops nystagmus, vomiting, or other untoward symptoms, the needle should be withdrawn. The resistance with which the alcohol enters is usually a reliable indicator as to whether the needle is in nerve tissue, provided, of course, that the position and depth are proper, as well as the definite radiation of pain. Should the patient complain of severe pain in the ear as the injection is started, it may mean the alcohol is entering the eustachian tube or has struck a small branch from the trigeminal which innervates the ear. Reference to Table IV, shows that of 600 alcohol injections, 345 or somewhat over half, were given to the third division.

TABLE IV.—NUMBER AND TYPE OF INJECTIONS

Type	No.	Per cent
3d division	345	56
2d division	98	16
Infraorbital	147	24.4
Supraorbital	12	1.8
Ganglion	12	1.8

The average period of relief from third division injections was 14.3 months, the shortest period being 9 months and the longest 8 years (cf. Table V).

TABLE V.—AVERAGE RELIEF FROM INJECTIONS WITH ALCOHOL

Division	Months
Supraorbital	6
Infraorbital	12.4
Maxillary	12.4
Mandibular	14.3

Second division injection. Trigeminal neuralgia involved the superior maxillary branch in 24.3 per cent of our cases. Pain may be controlled either by a deep injection at the foramen rotundum or at the infraorbital foramen, depending entirely upon its distribution. The infraorbital injection is usually sufficient if the roof of the mouth is not involved. Since this foramen is more accessible than the rotundum, such an injection is relatively simple and, therefore, more frequently chosen.

In doing the deep injection at the foramen rotundum, it is our custom to use only two of the described routes; the anterior approach, so called because the needle enters the pterygomaxillary fissure anterior to the coronoid process of the mandible, while posteriorly to the coronoid is the posterior approach. The anterior approach is more direct and usually more successful. However, at times, it is impossible to reach the pterygomaxillary fissure because of the overhanging edge of the maxilla, and in such patients the posterior approach may be easier.

The same preliminary procedures as in the third division injection are used for the deep second and infraorbital procedures, in that the patients are given no preliminary medication and the skin is sterilized with 70 per cent alcohol. In the anterior approach, the needle is pressed through the skin just beneath the anterior portion of the zygoma and anterior to the coronoid process, as shown in Figure 4. The needle passes medially at a 40 degree angle, anterior to the coronoid process, and immediately posterior to the maxillary process. As it enters the pterygomaxillary fissure, which is a narrow opening about 0.5 centimeter wide, it usually strikes the external pterygoid plate behind or the posterior border of the maxilla in front. The nerve, as a rule, is reached at 5.5 centimeters depending, of course, on the width of the face of the patient (see Fig. 3). It is important that one should not go deeper than 6 centimeters at any time, because of possible injury to important structures, especially the optic nerve. If the external pterygoid plate is struck, it can be used as a valuable landmark, the foramen rotundum lying anterior and 0.75 to 1 centimeter deeper. If the posterior portion of the maxilla is reached before entering

the pterygomaxillary fissure, it will also serve as a guide, keeping in mind that the fissure in which the nerve lies is bounded by the maxilla anteriorly and the external pterygoid plate posteriorly. By gentle manipulation of the needle, the nerve will be reached, if no unusual bony prominences make it impossible. Throughout the procedure, one should have a mental picture of the deep structures. As soon as the needle enters the nerve tissue, a spray of pain will be felt along the course of the nerve. Here, again, only a few drops of alcohol are injected at a time; if complete anesthesia of the upper lip, ala of the nose, and roof of the mouth is obtained, 1 or 2 cubic centimeters more is then injected slowly. The most reliable place to test the anesthesia obtained is on the upper lip and the ala of the nose, while the patient has the eyes closed.

When the roof of the mouth and gum is not involved, the infraorbital nerve is injected as it comes out of its foramen. This is relatively simple because of its position. It is located approximately 0.8 centimeter beneath the inferior orbital rim and 2.5 centimeters from the midline. Instead of having the face turned to one side, it is easier to have the face straight up. The index finger of the left hand is placed firmly over the inferior orbital ridge so as to avoid injuring the eyeball and surrounding tissue by having the needle slip over the bony rim. The point of the needle is then inserted into the nasolabial fold about 2.5 centimeters from the midline, directing it at a very acute angle toward the infraorbital foramen. As a rule one has no difficulty in telling when the tip of the needle enters the foramen. As it does so, the patient immediately complains of a spray of pain radiating to the ala of the nose, cheek, and upper lip. The alcohol is then injected, a few drops at a time, anesthesia usually resulting immediately. Frequently, however, the infraorbital nerve branches before it leaves the canal, thus making it necessary to probe gently until the tip of the needle enters. As it does so, the patient immediately complains of a spray of pain radiating to the ala of the nose, cheek, and upper lip. The alcohol is then injected, a few drops at a time, anesthesia usually resulting immediately. Frequently, however, the infraorbital nerve branches before it leaves the canal, thus making it necessary to probe gently with the tip of the needle and to inject a few drops each time the patient has a twinge of pain. During the procedure, it is a good policy to keep firm digital pressure in the immediate vicinity of the needle, preventing hematoma formation because injury to the infraorbital artery is at times unavoidable. Such pressure also prevents the backing up of alcohol in the superficial subcutaneous tissue. This is important as alcohol in this region may cause a drooping of the upper lip due to injury of the facial branches. In some individuals the bone covering the maxillary sinus is of paper thickness, thus allowing the point of the needle to enter the sinus with the least pressure. This happened once in this clinic without harmful results and probably would have been overlooked if bloody alcohol had not escaped from the nostril on the side of the injection as the patient stooped over to pick something up from the floor immediately following the injection. There have been 150 second division injections in our series, the average period of relief being 12.4 months, ranging from 6 months to 3 years (Table V).

The first division can be injected at the notch in the supraorbital ridge. The results are not as satisfactory as supraorbital neurectomy because the supraorbital nerves usually fan out over the supraorbital ridge, making it difficult to strike all the fibers with alcohol. Only twelve supraorbital injections were performed, the average relief from these being 6 months.

There have been occasional slight complications of alcohol injections such as hematomas, temporary dizziness, and headaches, and in one instance transient nystagmus and diplopia. Two patients had sixth nerve palsies lasting for an hour or two and one patient had temporary dilatation of the pupils after a third division injection. Only one patient was advised to enter the hospital and that was because of dizziness, nystagmus, headache, and diplopia following a third division injection in which the tip of the needle must unwittingly have entered the subarachnoid space surrounding the ganglion. The reason for this assumption is that the entire half of her face became anesthetic, lasting one hour. The patient was entirely well the next morning and had no ill effects.

The real objection to alcohol injections is that they give only temporary relief. The patient realizes that the pain will return sooner or later and is, therefore, more or less apprehensive of this fact. The other objections are that they are painful and in certain individuals the nerves cannot be reached properly because of scar formation from previous injections or because of abnormal bony protuberances, especially in the region of the foramen rotundum.

There are no contra-indications to alcohol injections with the exception of local infections in the skin or tissues through which the needle must pass.

Ganglion injections. In regard to injection of the gasserian ganglion itself, we feel that unless one has become especially proficient with this delicate procedure, it is probably more hazardous than the usual sensory root avulsion when the latter is carried out by a properly qualified surgeon. Relatively few attempts have been made to inject the ganglion in this clinic, the total number being twelve. They were done either because the patient refused operation or was physically unfit for operation.

Peripheral neurectomies are performed only when pains are limited to the supraorbital division. Two to four years' relief is obtained in this way. The procedure is very simple and may be repeated several times. The great advantage of this operation is that it avoids the dangers of keratitis that may follow a complete sensory root avulsion.

Sensory root operation. A rigid rule is followed in that no patients are operated on for section of the sensory root without making them thoroughly acquainted with the numbness of the face which will inevitably follow. This is done by giving at least one alcohol injection. The numbness itself is uncomfortable and the feeling cannot be appreciated by even the most intelligent patients until they have actually experienced it. When they have been made to realize that numbness of the face is infinitely better than the previous pain, or if injections become too difficult because of scar tissue, the radical operation is advised. The treatment of trigeminal neuralgia is one of election and therefore, if good results are obtained by alcohol injections which are entirely without danger in the hands of the experienced, there seems to be no particular reason for demanding that the patient have a sensory root avulsion. Several things, however, must be kept in mind and these are that, if the patient is young and has a severe major neuralgia, it is hardly fair to ask him to go through years of more or less painful alcohol injections. The knowledge that the pain is bound to recur and the necessity of resorting to an injection each time this happens, is by no means conducive to maintaining the proper frame of mind to compete in every day business. On the other hand, in many patients beyond the age of 70 years, a single injection may see them comfortably through their allotted span of life without resorting to a more radical procedure.

The technique used in the sensory root avulsion will not be described here as it is the same as that used by practically all neurosurgeons and several well illustrated articles have been written on this subject. The operation has been performed on 176 patients during the past 10 years without a fatality. In all instances, the temporal route was employed. The complications were minor with the exception of the rare development of keratitis in approximately 5 per cent of those in whom complete root avulsion was practiced, while perhaps another 5 per cent considered the subsequent paresthesia almost as bad as the original pain. Naturally, it is these patients that make the neurosurgeon hesitate in advising the radical operation without previously acquainting them with the numbness by alcohol injection. However, the great majority of patients are most appreciative and grateful, making the operation one of the most satisfactory that a surgeon can perform. A temporary facial palsy occurred in 6 patients during the earlier years, but this complication has not been noted during the past 5 year period. Whenever the first division has been included in the root resection, the most meticulous postoperative care of the eye cannot be too greatly emphasized. The patients on their discharge from the hospital are instructed to wear specially made glasses to serve to keep the cornea free from trauma and are given written directions as to the care of the eye if any suspicion of inflammation arises.

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END-RESULTS WITH THE WATKINS' INTERPOSITION OPERATION[1]

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THE treatment of uterine prolapse and cystocele in women past the menopause perhaps seems an old and time worn subject, for it is nearly 35 years since Watkins first described the method which we largely use for the treatment of such cases. A review of the recent literature and transactions of societies, however, reveals that gynecologists are still divided between more or less ardent advocates of this method and those who oppose it. Many of the opponents prefer the Mayo type of vaginal hysterectomy and some still use a combination of vaginal plastic repair with abdominal suspension of the uterus. No less than four articles upon various phases of this subject have appeared in a single journal[2] within a recent 6 months' period, ample evidence that the subject is still one of active current interest. In one of these articles Robert T. Frank states that he uses the interposition operation only occasionally in cases with large billiard ball cystocele and without marked prolapse. His most frequent procedure has been plastic vaginal repair and ventrofixation, but he reports only 66 per cent satisfactory results in a series of 414 cases. In the discussion of a report of "Two Cases of Pregnancy Following the Watkins Interposition Operation" by Dr. Carl H. Ill, of Newark, before the New York Obstetrical Society recently, Dr. B. P. Watson unreservedly condemned the procedure in the following words: "I believe that all of these complications could have been avoided had interposition not been done. I regard it as a bad operation." On the other hand, Coventry and Moe have reported 69 perfect anatomical results in 70 operations and in 66 all symptoms were entirely relieved. Laws, of Philadelphia, reported one failure in 33 operations.

We have found the interposition operation when used in properly selected patients a most satisfactory procedure. Dr. Thomas S. Cullen has been one of its most ardent advocates for years, and under his championship it has become very popular among most of the members of the department, though we do have one or two rather ardent advocates of the vaginal hysterectomy.

We restrict the use of the interposition to patients near, at, or past, the menopause, except in an occasional case where future childbearing is strongly contra-indicated. In such cases, of course a careful tubal sterilization is done at the time of operation. Following this rule we have had no cases of pregnancy in the past 18 years. Contrary to Ward, we do not find that the degree of prolapse matters and use the operation for complete procidentia as well as lesser degrees of prolapse.

Most of the members of the department restrict the use of the vaginal hysterectomy to those cases in which some uterine pathology makes hysterectomy advisable. In the younger women we use a combination of the necessary vaginal repair with abdominal suspension of the uterus, the Mayo modification of the Gilliam technique being used.

In the preparation of this paper I have studied the ultimate results of the interposition operations done during the years 1927–1931 inclusive, and also, for sake of comparison, the results in the much smaller series of vaginal hysterectomies done during the same period. There were 68 of the former and 26 of the latter operations done during this time. I have been able to obtain recent follow-up information on 48 of the patients who underwent interposition operations and on 17 of those who had vaginal hysterectomies.

Of the 68 patients who had interposition operations, all but 9 were 45 years old or older, and all but 9 were at or past the menopause. The oldest patient was 78, the youngest 26. Two patients were over 70 and two under 30.

Sixty of the patients were white and eight colored. We have noticed over a period of years in a clinic treating a large number of colored patients the relative rarity of conditions requiring vaginal plastic work in this race.

There was one nulliparous patient in the series and one in whom the number of children was not recorded. The average number of term deliveries was 4.3. Four patients had had ten or more children.

The symptoms of which the patients complained were the usual ones in such a group: backache, dragging sensation in the pelvis, dysuria, frequency, constipation and evidence of prolapse.

The extent of the various anatomical defects in the 68 patients is shown in the accompanying tables.

In addition to the interposition operation, the cervix was amputated in 48 patients. In all except 3 cases a perineorrhaphy and posterior colporrhaphy were done. In these 3 cases the perineal relaxation and rectocele were so slight as not to

[2] Am. J. Obst. & Gynec.

[1] From the Department of Gynecology of the Johns Hopkins University and Hospital. Paper presented before the Bay Ridge Medical Society, Brooklyn, New York, May 9, 1933.

TABLE I.—DEGREE OF PROLAPSE

Degree of prolapse	No. of patients
None (large cystocele)	4
First degree	18
Second degree	33
Complete procidentia	13

TABLE II.—SIZE OF CYSTOCELE

Size of Cystoceles	No. of patients
Small	3
Moderate	11
Large	54

TABLE III.—SIZE OF RECTOCELE

Size of Rectocele	No. of patients
None	1
Small	16
Moderate	22
Large	29

require repair. Tubal sterilization was considered advisable and was carried out in 6 patients.

The operations were performed by 11 different operators. Thirty-five of them were done by 5 different members of the visiting staff and the 33 remaining by the various residents and assistant residents during the period under consideration. This fact disposes of any criticism or objection that might be offered that the operation is one capable of being performed only by operators of long experience and superior skill, for, while the residents and assistant residents in our department are all men with 4 to 5 years of thorough postgraduate training in pathology, anatomy, and surgical technique, they are still serving an apprenticeship in gynecological surgery.

RESULTS

One of the 68 patients died of pulmonary embolus during postoperative convalescence. The 67 others were discharged as well, so far as their gynecological conditions were concerned, after an average convalescence of 22 days. This perhaps may impress some as a rather prolonged period of postoperative convalescence, but our attitude in the treatment of such cases is that we are dealing essentially with a hernia, and that one of the most important factors in treatment is to relieve the repaired structures of all possible strain until ample time has elapsed for thorough healing. We, therefore, make it a practice to keep such patients in bed for fully 2 weeks following the operation and then permit them to get up and about very gradually over a period of several days.

Of the 67 patients discharged, we have been able to obtain recent data on the ultimate result in 48. Of these all but 2 had excellent anatomical

TABLE IV.—AMOUNT OF PERINEAL RELAXATION

Relaxation	No. of patients
Slight	1
Moderate	21
Marked	43
Third degree laceration	3

TABLE V.—WATKINS' INTERPOSITION OPERATION AND VAGINAL HYSTERECTOMY—END-RESULTS

	Interposition		Vaginal hysterectomy	
	Number of patients	Per cent	Number of patients	Per cent
Number of operations	68		26	
Number followed	48		17	
Perfect results	32	66.6	8	47
Satisfactory results	14	29.2	4	23.6
Unsatisfactory results	2	4.2	5	29.4

results. In 2, after 5 years of complete relief, there was recurrence of moderate prolapsus. In both of these the original prolapsus was of the second degree. None of the 10 patients followed who were originally suffering from complete procidentia has had a recurrence. In 4 patients with perfect symptomatic results and perfect cure of cystocele and prolapsus, it was found on examination that there was still slight rectocele above the perineum. In these the posterior repair was probably not carried sufficiently high to reduce the rectocele completely but as the patients were entirely free from symptoms the results may be considered satisfactory. Three patients complained of dyspareunia. In all of these the result of the interposition was perfect, but a too extensive perineorrhaphy had resulted in a rather small introitus. Nine patients still complained of some frequency and dysuria. In 1 of these the symptoms were due to the presence of a urethral caruncle which has been removed by fulguration with subsequent relief. The others had all had considerable frequency and dysuria before operation and the symptoms, though still present, have been much less annoying since. Four of them had definite urinary infections for which they received treatments. In summary then we may say that 2 cases may be considered unsatisfactory because of recurrence after 5 years. In 32 the results have been perfect anatomically and symptomatically. In 14 the results have been satisfactory but cannot be considered perfect because of slight residual symptoms or slight anatomical defects not really associated with the interposition.

In 1922 Shaw reported the results of the same operation for the same clinic up to that time. He

was able to obtain data on only 58 of 118 patients. Of these 21 had been operated upon since 1915 and among these 21 there was 1 failure. Among those patients operated upon prior to 1915, he found 12 failures, but it is quite evident from his report that in the earlier years the careful selection of patients as regards age, etc., now practiced was not adhered to. For instance, 34 of his patients were under 40 years of age.

Brady, in 1925, reported a series of 48 followed patients operated upon by Dr. Thomas S. Cullen. In 47 of these the result was entirely satisfactory while in one there appeared after 10 years a recurrent prolapse of the anterior vaginal wall. This was repaired with excellent result.

If now we add Shaw's 21 patients since 1915, Brady's 48, and the present series of 48, we have a total of 117 properly selected patients treated by this method in whom evidence of recurrence could be found in only 4, or approximately 3.5 per cent. In my smaller series the 2 failures give a percentage of slightly more than 4 per cent.

Now let us consider for a moment the smaller series of 26 vaginal hysterectomies done during the years 1927 to 1931 inclusive. These 26 operations were done by 9 different operators; 14 of them were done by 4 members of the visiting staff, and the 12 remaining by the 5 residents during this period. Equal care was exercised in the selection of these patients for operation as in the preceding group. The patients with one exception were all near or past the menopause. This one was 34 years of age and in addition to descensus and a large cystocele had been suffering from persistent menorrhagia for 2 years. The oldest patient in the series was 70; the average age was exactly 50. In 13 of the patients the operation was chosen in preference to an interposition because of some uterine pathology requiring removal of the uterus, and in the 13 remaining it was the operator's preference.

In 11 of the patients the prolapse was of first degree, in 7 of the second degree, and in 8 there was complete procidentia. The 26 patients were all discharged as well after an average convalescence of 25 days. This increased average of convalescence is due to three patients whose convalescence was greatly prolonged by complications. One of these had bronchopneumonia, another had bilateral thrombophlebitis, and the third developed a rectovaginal fistula, which was later successfully closed.

We have been able to obtain recent data on 17 of the 26 patients. In 12 the anatomical result was good, while 3 showed recurrent cystocele, and 2 others prolapse of the vaginal vault. In one of the latter there was also a large enterocele. Of the 12 with good anatomical result, 4 complained of urinary symptoms.

We have then practically 30 per cent of anatomical failures with vaginal hysterectomy as opposed to approximately 4 per cent anatomical failures with the interposition operation. The criticism cannot be offered that the failures with the vaginal hysterectomy were due to inexperience of the operators, for 2 patients in whom failures occurred were operated upon by the same operator and 2 others by another. Both of these men are surgeons who have had long experience and have superior skill and one of them is probably the most ardent advocate of the procedure to be found in the department.

In summary, then, I believe I am justified in saying that in our experience the Watkins' interposition operation is the procedure of choice for the treatment of prolapse of the uterus in women past the menopause. It is preferable to a combination of vaginal plastic with abdominal suspension because it is a shorter and simpler procedure and avoids the increased risks incident to laparotomy. The combined operation, however, is the procedure of choice in women during the childbearing period. The interposition is preferable to the vaginal hysterectomy because, in our experience at least, it gives better permanent results, it is easier to perform, and, in cases in which there happens to be a recurrence, a second repair is much simpler with the uterus still present. We can find no reason for considering an advanced degree of prolapse a contra-indication for interposition, for in all cases with complete procidentia whom we have been able to follow the results were perfect. We believe that vaginal hysterectomy finds its chief use in cases in which a repair is necessary for the cure of cystocele and prolapse, and the removal of the uterus is at the same time indicated.

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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SEPTEMBER, 1935

DIVERSION OF URINE ABOVE LEVEL OF BLADDER

IN the not too distant past a very considerable number of patients with bladders wrecked beyond repair have either lived in grave discomfort or even torture, or gone to their deaths from renal insufficiency and infection. During the past 15 years much attention has been paid to various methods of diverting the urine; all of them presenting some difficulty, and therefore requiring a considerable period of study in order to assess their value. Although there are many patients for whom such procedures are desirable, the number coming under the observation of any one surgeon is rarely large enough to warrant conclusions except after the lapse of considerable time. Furthermore, we are concerned here not with immediate results, not with mortality, but with morbidity and late quasi-permanent results. The lapse of time and the accumulated experience seems to me now to warrant some statement in regard to the place of these various procedures.

Granting at the outset that the bladder is either worthless, as in the cases of the extreme congenital deformities of exstrophy and complete epispadias, or damaged beyond repair by inflammatory processes, such as chronic interstitial cystitis and tuberculosis, or threatening death from a lesion of its own, as in the case of cancer, some diversion of the urine with or without cystectomy—indicated rarely except for exstrophy and cancer—is clearly indicated.

We have at our disposal three methods: nephrostomy, uretero-enterostomy, and cutaneous ureterostomy.

Nephrostomy may be used as an intermediate step in the re-arrangement of damaged ureters in which temporary diversion is indicated. It is, I believe, rarely the best method for permanent diversion, since it is not notably more certain to preserve the integrity of the kidney and is more inconvenient than cutaneous ureterostomy.

There remain, therefore, the two other methods, implantation into the bowel or implantation into the skin. It is interesting to note that the mortality and immediate results of uretero-enterostomy have apparently been importantly better in the United States than in Europe, where the operation has been considerably abandoned by many eminent experts on the ground of its high mortality, which has often been in the neighborhood of 30 per cent. As compared with this there are considerable series of cases in this country showing a mortality below 5 per cent. This difference has arisen, I think, from the different selection of patients. Space does not here permit a discussion of the principles of selection, but it seems to me quite clear that the cases suitable for uretero-enterostomy will be almost invariably those in which the ureters are substan-

tially normal, and that the attempt to transplant grossly abnormal ureters is likely to be followed by a much higher mortality and less satisfactory results.

For patients with normal ureters, where the operation can be done by moving one ureter at a time, the mortality and immediate results are satisfactory. The morbidity and end-results, although still in doubt, show, I believe, that the kidneys continue to function reasonably satisfactorily over periods in excess of ten years. On the other hand, there is no convincing array of cases showing that the kidneys remain strictly within normal limits after transplantation of the ureters by any method. We ought not to assume on the basis of the present evidence that uretero-enterostomy enables the patient to continue indefinitely with an entirely normal upper urinary tract. Some degree of dilatation almost universally associated with some degree of infection is the rule.

For the patients with grossly abnormal ureters, cutaneous ureterostomy has, I think, been shown to have a lower mortality and a relatively satisfactory result. Many of these patients already have infected kidneys. All of them—by definition—will have some dilatation of pelvis and calyces. If the operation is technically well carried out, and particularly if a fair sized catheter is kept permanently in the ureter up to the level of the renal pelvis, these patients are dry, comfortable, and can live effective lives.

Briefly summarized, nephrostomy is at its best in draining the kidney while some rearrangement of the ureter can be planned. Uretero-enterostomy is at its best where the ureters are normal, and will be most useful in congenital anomalies, in certain injuries of the bladder, and in a few cases of chronic interstitial cystitis. It may be used as a preliminary to total cystectomy for cancer, but will here carry a higher mortality, since both ureters must be moved at the same time, and it is desirable to do the cystectomy either at the same sitting or after a brief interval. This is a grave surgical undertaking. Cutaneous ureterostomy is at its best in cases in which the bladder has ceased to be useful as a result of intolerable tuberculous cystitis, in other types of inflammation with dilatation of the ureter, in some cases of neuromuscular dysfunction, and in those cases of cancer of the bladder in which, although the ureters are obstructed and dilated, relief is still worth trying for or total cystectomy is still regarded as possibly curative.

HUGH CABOT.

A NEW BLOOD SUPPLY TO THE HEART BY OPERATION

THE human heart entered the domain of surgery in 1895 when Cappelen sutured a stab wound, the first operation of its kind on a human being to be recorded. At that time the attitude of the profession toward this operation was not uniformly favorable. Stephen Paget felt that surgery of the heart offered no prospect for development. This attitude can be understood when one contemplates the opportunities for the development of operative surgery offered by other organs during that early part of the aseptic period. Why should one be interested in the heart as a surgical organ when there were so many fruitful fields of endeavor? And so the decades have gone by. What has been accomplished in cardiac surgery has to a large extent been the result of sporadic interest. A few important contributions have been made, but in general it can be stated that the heart has not received very much sustained study by surgeons. The reason for this dearth of surgical endeavor is obvious. What could one hope to accomplish in this field!

My associates and I have worked with the problems of cardiopericardial surgery for a dozen years. For a long time it seemed as though we were working in a blind alley and all that we could accomplish in the first few years was to make observations and from this study to formulate a point of view concerning surgical problems.[1] One of these observations was to note the presence of blood vessels in tissues that were adherent to the heart, an observation of no special significance at the time it was first made. After the lapse of several years a band of scar extending from the left ventricle was transected in a human patient. Brisk bleeding occurred from each cut surface. Here was evidence, the first of its kind to be recorded, that adherent tissues could and actually did transport blood to the human pulsating heart. A new significance was attached to this observation because in the intervening years we were attempting to give the myocardium a new source of blood supply.

According to our point of view, the correctness of which seems quite obvious, the heart is anchored in the body. It is anchored by the walls of the great vessels, by a little fat, a few nerves and a few lymphatics, and these structures are relatively avascular tissues. Because of this anatomical arrangement the heart has been deprived to a great extent of an important compensatory property, namely, the ability to develop a collateral circulation to meet an emergency, to preserve life during the first few moments, hours, days, and weeks after a serious coronary accident. The appalling incidence of sudden death in our adult population attests to the destructive nature of coronary closure.

The experiments on this subject, done in collaboration with Dr. V. L. Tichy and Dr. Alan R. Moritz, consisted of the destruction of the mesothelial envelope around the heart and the construction of a vascular bed from which the heart could obtain a new source of blood supply. In these experiments the epicardium and mesothelial lining of parietal pericardium were removed. Tissues were then brought into contact with the myocardium. These tissues consisted of fat, fibrous pericardium, pedicle grafts of skeletal muscle and omentum. A physiological need for blood in the myocardium was produced by occluding the coronary arteries by silver bands which were placed around the arteries close to their aortic ostia. These bands were compressed in successive stages until the arteries were completely occluded. Complete occlusion of both coronary arteries was achieved experimentally with recovery, and when the extracardiac vascular bed was injected with dye the myocardium became diffusely and intensely stained. It was concluded from these experiments that the heart was given a new source of blood supply.

Supplementary facts bearing upon the subject were established by experiments conducted in collaboration with Dr. Ernest Bright and Miss Alice B. Maltby. It was shown by these experiments that the presence of a collateral vascular bed adherent to the myocardium protected the heart against sudden occlusion of the right coronary artery. The degree of protection was not always sufficient to withstand complete occlusion of this artery in one stage, but the collateral bed had some prophylactic effect. When the ramus descendens of the left coronary artery was occluded in one stage, the prophylactic effect of the vascular bed was less marked. It was concluded from these experiments that the larger the coronary artery occluded, the less the prophylactic effect.

It was also found that the right coronary artery, the descending ramus of the left or the

[1] It may be of interest to note that over 1200 operations on the heart have been carried out in the Surgical Laboratory of the Western Reserve University School of Medicine.

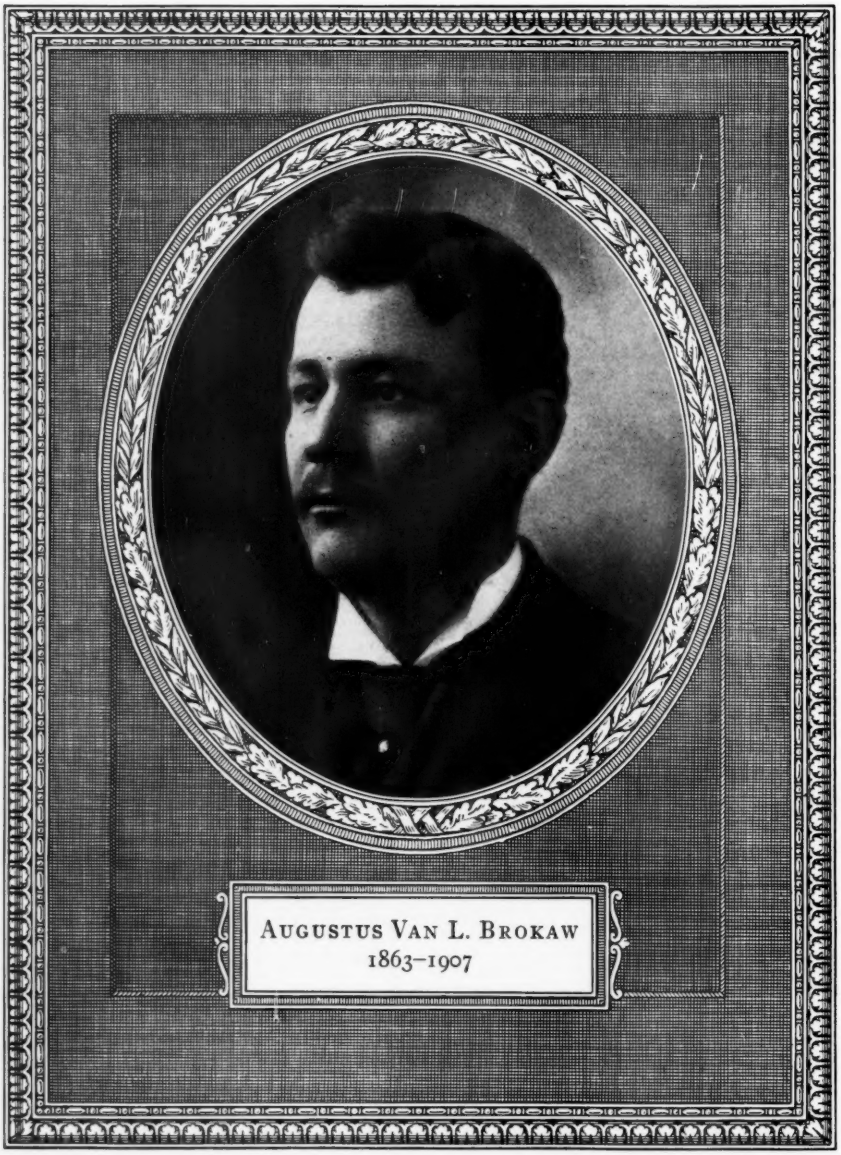
circumflex ramus of the left coronary artery could be ligated with almost uniform success if the occlusion were carried out in two stages. It was also learned by experiment that localized ischemia of the myocardium was highly fatal. Ligation of four or five peripheral branches of the coronary arteries over the apex of the left ventricle was uniformly fatal. The reduction in coronary blood flow brought about by this type of peripheral ligations was not great when compared to the total amount of blood passing through both major coronary arteries. A much greater reduction in the total coronary blood flow could be tolerated by the heart provided the constriction of the arteries was central rather than peripheral. This observation introduced the subject of distribution of blood flow in the heart—a subject of vital importance. The following demonstration was carried out. A collateral bed was applied to the myocardium and the right coronary artery was occluded completely. Several months later the left coronary artery was injected with dye. In this experiment the dye spread diffusely throughout both ventricles, while in a normal heart the dye did not penetrate the wall of the right ventricle. Not only was the right ventricular wall injected with dye but the dye flowed freely from the cut surfaces of the collateral bed. From this type of experiment it can be stated that the collateral vascular bed not only can bring blood into the myocardium from extracardiac sources but also it can transport blood from the bed of a coronary artery where the circulation is good to the bed of an artery where the circulation is deficient. In this respect the collateral bed can function as an anastomotic bridge which can bring about an equal distribution of blood to various parts of the myocardium.

During the last two years a series of experiments has been carried out in collaboration with Dr. Robert Hosler and Dr. John Williams concerning the effect of adhesions upon the heart. While this work is still in progress, nevertheless, it can be stated that intrapericardial adhesions are silent, i. e., they produce no clinical manifestations of circulatory embarrassment. It can also be said that extrapericardial adhesions are silent, and that while both of these lesions combined can increase the work load of the heart, still these combined lesions usually, but not always, are silent. A second way in which extrapericardial and intrapericardial adhesions combined can affect the circulation is by angulating the heart from its normal axis. A third possibility is by the development of cardiac compression, but in this condition the compressing scar is the detrimental factor while adhesions, when present, are entirely silent and incidental. In general it can be stated that the importance of cardiac adhesions has been greatly overemphasized in the past. In most cases they produce no circulatory embarrassment whatsoever.

With these experimental data as a background, it was decided to try to apply them to human patients. The operation, the first of its kind, was done February 13, 1935. The insertion of the left pectoral muscle was incised to mobilize the muscle. The muscle was also cut to the left of the sternum. The epicardium was removed as was also the lining of the parietal pericardium. The pectoral muscle and the left internal mammary artery were brought onto the surface of the heart. Over five months have elapsed since this operation was carried out, and the patient claims that he is better. His feeling of substernal oppression has disappeared. He states that the sharp pain down the left arm has disappeared, that his feeling of impending death has gone. He is now employed as a gardener. I have carried out the operation in three additional patients. These patients tolerated the

operation, although one developed a thrombosis on a calcified plaque at the bifurcation of the aorta a week after the operation. The other two are living and apparently improved. Up to the present time we have had no deaths from the technical aspects of the operation.

In conclusion it should be said that while the myocardium has been given a new source of blood supply experimentally, it cannot be said that the experimental data have been adequately applied to patients suffering from coronary sclerosis. The operation will have to be applied to a number of patients before it will be known how beneficial it will be. Until this has been accomplished, the operation should be looked upon as an experimental procedure. It is my belief, however, that this operation is going to open up a new field of surgery. It was my desire to withhold presenting this work until the results of the operation as applied to patients were definitely known. Unfortunately this was not possible. The operation is not without hazard, and it is my sincere hope that surgeons will not accept and apply this operation to human patients until the results are known. CLAUDE S. BECK.



AUGUSTUS VAN L. BROKAW
1863–1907

MASTER SURGEONS OF AMERICA

AUGUSTUS VAN LIEW BROKAW

THOSE of us who have been privileged to develop into surgeons of reputable standing must acknowledge a definite debt of gratitude to certain of our former elders in the profession. Our appreciation of their inspirational influence is cherished even after the purely technical knowledge taught by them has become more or less obsolete. Such is the impelling motive which led to the writing of this short biographical sketch.

Augustus V. L. Brokaw was born in the St. Louis City Hospital on April 6, 1863. His father, Dr. F. V. L. Brokaw, was at that time the resident superintendent and surgeon in charge of that institution, but resumed his private practice in the city a year or two thereafter and became a very successful physician.

The boy did not especially distinguish himself for being studious during the years of his preliminary education; yet, when he found his proper sphere in the study of medicine, applied himself so assiduously that he graduated with the highest honors in the Class of 1885, from the Missouri Medical College. Then according to the then approved procedure for embryo-doctors he spent about 2 years in the European surgical clinics. Still, the most forceful constructive factor of his career was encountered upon his return to the city of his nativity. There his locally influential father had arranged with Professor Theodore F. Prewitt to accept the son as an assistant of a preferential kind.

Dr. Prewitt was surgeon in chief to St. John's Hospital, and Brokaw soon demonstrated his ability to the several successive superiors and superintendents of that Roman Catholic Charity of the Order of the Sisters of Mercy. It took them but 4 or 5 years to recognize the superior talents of their junior surgeon. From then on, A. V. L. Brokaw was the surgical favorite of the hospital, because he had brought a wealth of surgical knowledge from Berlin and Vienna, which was greatly augmented by the daily association with Professor Prewitt, who was noted for his ability to teach and who had an abundance of clinical material at his service.

Meanwhile Brokaw was also demonstrator in anatomy at the Missouri Medical College under Professor Herman Tuholske, and succeeded the latter as professor of anatomy and operative surgery in 1891. In 1899, when this institution united with the St. Louis Medical College to become the Medical Department of Wash-

ington University, he took the chair of clinical surgery; and, when Dr. Prewitt retired in 1902, Dr. Brokaw was chosen surgeon in chief to St. John's Hospital, which was also affiliated with Washington University.

Then, in 1903, the St. Louis University established its School of Medicine by purchasing the Marion Sims-Beaumont Medical College, and immediately sought the assistance of several Roman Catholic hospitals in providing clinical instruction for its students. The control of the medical staff of St. John's Hospital was promptly and properly transferred to the administration of the newly acquired Jesuit school, and Dr. Brokaw accepted the chair of clinical and operative surgery in the St. Louis University Medical School and thereby remained at the hospital as its surgical chief. He retained these connections until he died suddenly 4 years thereafter, of a gastric hemorrhage, on January 25, 1907.

When the street railways of St. Louis were fused into one huge organization Dr. Brokaw had already functioned as surgeon for several independent street car lines; and, although still "in the thirties," he was appointed chief surgeon to the citywide transit system. A half dozen or more of his full time assistants were housed in the spacious office building attached to his residence, first at Compton Avenue and Washington Boulevard, and later in more commodious quarters on Taylor Avenue. By day and night some of these were always ready to answer emergency calls. Then, too, there were scores of privately practicing physicians distributed throughout the area of St. Louis who had been appointed for part time duty. On the whole, this corps was quite efficient.

Brokaw installed an X-ray apparatus almost immediately after he saw Professor Charles O. Curtman first demonstrate the new discovery of Professor Roentgen in Professor Nipher's laboratory at Washington University in 1896. He foresaw its great value to medicine, and especially to industrial and traumatic surgery. On account of the frequent changes and improvements in the early models of coils and tubes he was kept busy discarding various pieces of apparatus and replacing them with others of greater efficiency. His name should be inscribed high up on the honor roll of pioneer roentgenologists.

A. V. L. Brokaw was a stickler in asepsis, by enforcing thorough heat sterilization of surgical instruments, linens, etc., to obtain an aseptic operative field at a time when most surgeons were still indifferent or careless in such matters. These precautions, coupled with the confidence in his own dexterity with a scalpel and his extensive knowledge in anatomy, are responsible for many recoveries which might have terminated otherwise. He had many admirers among the younger physicians, and was a popular consultant and operator with them.

Sometimes brusk and apparently blunt in demeanor, our subject was decidedly cordial and communicative to whomever he trusted and respected, even if that individual was his junior by many years. In his private work, as well as in his corporate practice, the question of remuneration was always secondary

to the aim to give everybody the utmost quantity and degree of service. Among the makers of medical history in 1935, some of his pupils and assistants are still diffusing the inculcated spirit of this short lived master who displayed a domineering attitude over his surroundings, which had the semblance of a small empire, and in which he played the rôle of supreme ruler. Nevertheless, in true regal fashion, he always assumed the full legal and moral responsibility for all personal acts, as well as those of every subordinate person in his service.

Removed as he was by death at the early age of not quite 44 years, it cannot be expected of him to leave a long literary record of his achievements and experiences. Thus Brokaw's published writings are comparatively few, but they are characteristic and reflect his progressive boldness of opinion on the important surgical problems at the end of the nineteenth and during the early years of the twentieth century.

ROBERT E. SCHLUETER.

LANDMARKS IN SURGERY

NICHOLAS SENN'S WORK IN EXPERIMENTAL SURGERY AND SURGICAL PATHOLOGY, AND ITS INFLUENCE ON THE SURGERY OF HIS TIME

ARTHUR DEAN BEVAN, M.D., F.A.C.S., CHICAGO, ILLINOIS

THE work of Nicholas Senn is an important landmark in American surgery. It is my purpose to present a brief sketch of the late Nicholas Senn and his work in experimental surgery and surgical pathology and its influence on the surgery of his time. I am delighted to do this as I knew Senn very well and followed with great interest his surgical work, both his research work and his teaching, in the period that I was an associate of his in the Rush Medical faculty from 1888 to the time of his death in 1908. Senn had a striking personality. He was a fine looking man of medium height, large head and large torso, and gave one the impression of great physical and mental power.

Garrison who has written such an admirable history of medicine gives the following brief account of Nicholas Senn:

> Nicholas Senn (1844–1908), of Buchs, Switzerland, settled in the United States in 1852, graduated from the Chicago Medical College (1868), and became professor of surgery at the Rush Medical College of that city. Senn was a highly trained, scientific surgeon, who made valuable experimental contributions to the study of air embolism (1885), the surgery of the pancreas (1886), gunshot wounds, and intestinal anastomosis, in which he introduced the use of decalcified bone plates. He was, in fact, a great master of intestinal surgery, especially in the surgical development of the treatment of appendicitis. He devised a method of detecting intestinal perforation by means of inflation from the rectum with hydrogen gas (1888), and was the first to use the roentgen-rays in the treatment of leucemia (1903). Senn played an important part in the Spanish-American War, founded the Association of Military Surgeons of the United States (1891) and, at his death, left a fine collection of medical books to the Newberry Library, and other handsome bequests to the city of his adoption.

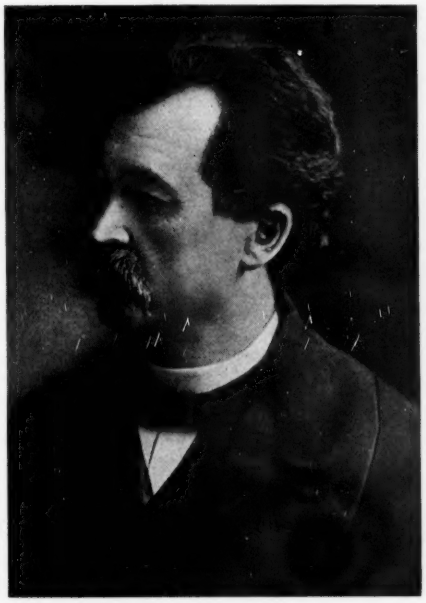
In 1887, following the death of Moses Gunn, the professor of surgery at Rush Medical College, Nicholas Senn and Charles T. Parkes were elected to succeed him. Senn's career had been an interesting one. After he graduated from medical school and after serving his interneship at the Cook County Hospital, he had gone to a small town in Wisconsin where he began the practice of medicine. From there he moved to Milwaukee where be built up a very large general practice and at the same time established a reputation as an excellent surgeon. In 1877, he went to Munich where he received training in surgical pathology and clinical surgery. After his return to Milwaukee he came to Chicago twice each week to give a clinic on the principles of surgery at the University of Illinois Medical School. At the same time he began his experimental work in connection with gunshot wounds of the abdomen, intestinal repair, and surgery of the pancreas. Together with Parkes he did a great deal to solve the problem of the proper handling of gunshot wounds of the abdomen. The report of his large series of experiments upon the repair of abdominal wounds was published in the *Annals of Surgery*. In addition Senn developed various plans of diagnosis in intestinal lesions; a very ingenious one being to inflate the bowel from below with hydrogen gas and then locating the intestinal tear by lighting the escaping gas. At the same time he was engaged in experimental work which led to the development of his celebrated bone plates.

In 1887, Senn spent 4 months visiting the important English, Scotch, and European clinics and wrote letters presenting quite fully his experience in these various clinics to his great friend, Christian Fenger. Christian Fenger had these letters printed in the *Journal of the American Medical Association*. After his return the American Medical Association published a little volume of these letters, entitled "Four Months Among the Surgeons of Europe."

In order to form a good conception of Senn's work and Senn's career, I think it is necessary to visualize the stage of the development which surgery had reached in Senn's time. Senn graduated from the Chicago Medical College in 1868, one year after Lister had published his first paper on antiseptic surgery, that was in 1867. Before that time surgery and medicine were in a fog, in a mist; one could not say that medicine was yet a science; but with Lister's work we had at last a scientific foundation upon which to build surgery. It should be remembered that when Lister presented his conception of antiseptic surgery it was but a theory based on Pasteur's demonstration that fermentation was a result of minute organisms. Influenced by this demonstration of Pasteur, Lister came to the conclusion that suppuration was due to the introduction of minute organisms into an open wound. He knew from experience that in a closed fracture suppuration did not occur, that in a compound fracture suppuration was the rule. He believed that in the open fracture minute organisms floated from the air into the

wound or were introduced into the wound by contact with the fingers or dressings or instruments that come in contact with it. Younger men can hardly realize the opposition, even the ridicule, that met Lister's suggestions.

Although Lister's paper on the antiseptic treatment in surgery was published in 1867, his suggestions were only very slowly accepted. Lucas - Championnière in France and Thiersch and Volkmann in Germany adopted Listerism in the early seventies. Lister's work was based at first upon the theory that germs produced suppuration and he sought to exclude them from the wound. These pus germs were not demonstrated until Ogston, in 1881, Rosenbach, somewhat later, and Koch, finally, with solid media were able to grow pure cultures of staphylococci and streptococci and prove conclusively the fact that these pus organisms were the cause of suppuration. In this uncertain period of about 15 years, the majority of the surgeons of the world refused to accept Lister's theory.



Nicholas Senn, 1844-1908

In looking over the literature of the period when Senn began his surgical work, in order to visualize the surgery of this time, I find nothing that compares with a publication of Billroth's in which he reports the work which he did in his surgical clinic at Zurich and his surgical clinic in Vienna from 1860 to 1876. (*Chirurgische Klinik*, Dr. Th. Billroth, Berlin, 1879.) During the sixteen-year period covered in Billroth's report he handled 9,508 cases and had 785 cases of erysipelas and pyemia and a few cases of tetanus, making about 8 per cent of accidental wound infections. Of 1,076 patients who died, 477 died of wound infection. He operated on 77 patients with breast carcinoma and removed the mammary glands with the axillary glands; of these 77 patients, 24 died, 3 from secondary hemorrhage, 1 from pneumothorax on the evening of the operation, and 10 each from erysipelas and pyemia. In his report on his amputations, resections, and osteotomies of the extremities, he operated on a total of 214 cases; of these 150 recovered and 64 died; 9 from collapse, 3 from erysipelas, 2 from delirium tremens, and 50 from septicopyemia—a mortality of 29.9 per cent. Billroth reports that up to February, 1879, he had done 140 ovariotomies; of these 83 patients recovered and 57 died—a mortality of 40.71 per cent. With this terrible mortality we wonder how the surgeons of 1880 had the courage to continue to operate. What a marvelous revolution was brought about by Lister! What a change came with the general introduction of sound antiseptic surgery!

In 1889, on his return from abroad where he had had the opportunity of studying bacteriology, Nicholas Senn published an admirable book on surgical bacteriology which ran through several editions and a year later published his textbook on *Principles of Surgery*. I am quite sure that this book had a very important bearing on the development of American surgery. It was the first book of its kind published in English. In Germany admirable books on the "Principles of Surgery" had been published by Koenig and Billroth. Many of our American and English surgeons devoted their time almost entirely to the practical side of surgery and had neglected the underlying principles. I remember John Chiene (professor of surgery at Edinburgh), whom I met shortly after this volume was published, told me that Senn's book on *Principles of Surgery* had led him to change completely his course of surgical instruction at Edinburgh and he adopted the book as the textbook for his classes. Senn later published a book on *Tumors, Their Surgical Aspects*.

The years from 1880 to 1900, which cover the most important period of Senn's career, were the two decades which witnessed the great development from the old surgery into modern scientific surgery, and Senn took a more important part in this development during these 20 years than any other American surgeon. Senn was considered for the position of professor of surgery at a number of institutions; among others, for the chair of surgery at Johns Hopkins when they were first organizing their faculty and before Halstead received the appointment, and later for the professorship at the University of Pennsylvania.

After he was made the head of the surgical department at Rush Medical College, Senn gave one of the most instructive clinics I have ever listened to. He was perfectly familiar with many of the best surgical clinics in Europe and in Great Britain, and he modeled his own clinic after the surgical clinics of the German universities. He gave two clinics a week. They began promptly at two o'clock in the afternoon. The large upper amphi-

theater at Rush College which had a seating capacity of about four hundred was as a rule crowded with students and visitors. Senn would first show gross and microscopic specimens from cases in which operation had been done usually at the preceding clinic. He laid great stress on a thorough knowledge of surgical pathology and bacteriology, then he would present patients from the hospital and the dispensary, make careful examinations and diagnoses, and would discuss the treatment which he thought was indicated in each case. This work would fill the time from about two to four o'clock. Then he would begin operating and, as a rule, had a long list of cases, three, five or seven, and he would continue operating until six o'clock, sometimes even until seven o'clock, and the majority of the students and visitors would remain throughout this long clinic. These clinics were always found to be most instructive and profitable.

Senn was very familiar with medical history. He had traveled so extensively through European countries that he had met personally many of the prominent surgeons so that he could give a very good presentation of the history of an operation, the man who had introduced it, and the results which he had obtained, so that one could visualize from his clear cut discussion very clearly the evolution of modern surgery. Senn also introduced into the clinic the plan which is customary in the German clinics of calling down student consultants, having them examine personally the cases, stating what they had found, their diagnoses, and their suggestions as to treatment. Senn constantly emphasized the importance of surgical research and experimental surgery in the development of clinical surgery.

Senn was very positive in his statements and gave very definite directions in regard to diagnosis and therapy. Some men considered this a fault; as a matter of fact it was an evidence of strength because a great surgical teacher must be definite, clear, and emphatic, if he is to be of the greatest service to his students. Lord Moynihan, who is probably more familiar than any other British surgeon with American surgery, stated recently in discussing American surgery that the two greatest teachers of surgery in America he had met were Nicholas Senn and John B. Murphy.

A prolific writer with a list of 316 books and articles to his credit, Senn presented the greater part of his work before meetings of the various medical and surgical associations in this country and abroad. Taking part in a symposium upon peritonitis, Senn stressed to his colleagues the importance of early operation; the removal of the source of the peritonitis; the advantages of rapid operation, and the startling improvements to be obtained from the use of large amounts of fluids administered subcutaneously. It is interesting that when at this date one reads his works, a picture of modern scientific surgery is presented far beyond the boundaries of the common surgical practice of his time. The surgical profession in this country should be proud of Nicholas Senn and of the great service which he rendered to medicine and surgery.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

ROBERT B. GREENOUGH, Boston, *President* DONALD C. BALFOUR, Rochester, *President-Elect*

HOWARD C. NAFFZIGER, *Chairman;* THOMAS F. MULLEN, *Secretary, Committee on Arrangements*

PRELIMINARY PROGRAM FOR THE 1935 CLINICAL CONGRESS

FOR the twenty-fifth annual Clinical Congress of the American College of Surgeons, to be held in San Francisco and Oakland, October 28–November 1, the surgeons of that great medical center on the Pacific coast have organized under the leadership of a strong and representative committee and have prepared a program of clinics and demonstrations that will provide a complete showing of their clinical activities in all departments of surgery. The Committee on Arrangements has been assured of the hearty co-operation of the clinicians at the medical schools and twenty-seven hospitals that will participate in the program.

The clinical program, published in tentative form in the following pages, is to be further revised and amplified during the coming weeks as the work of the program committee progresses. Operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 28, beginning at 2 o'clock, and for the mornings and afternoons of each of the four following days. The real program will be published daily during the Congress—a complete and accurately detailed program which will be posted in the form of bulletins at headquarters each afternoon for the succeeding day. The same material will be issued in printed form the following morning.

Special features of the clinical program include: (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray; (2) fracture clinics demonstrating modern methods of treatment; (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation of injured patients by surgery and physiotherapy.

Surgical motion picture films, both sound and silent, will be exhibited daily at headquarters at the Fairmont Hotel. Such surgical film exhibitions have met with popular acceptance in recent years, and an extensive exhibit, including many new films, is planned for this year's Congress.

EVENING MEETINGS

A tentative outline of the programs for five evening sessions, as prepared by the Central Executive Committee, is presented in the following pages. At the presidential meeting on Monday evening in the War Memorial Opera House the retiring president, Dr. Robert B. Greenough, of Boston, will deliver the annual address followed by the inauguration of the new officers — Dr. Donald C. Balfour, Rochester, Minn., president; Dr. Arthur W. Allen, Boston, and Dr. John A. Gunn, Winnipeg, vice-presidents. The annual oration on surgery will be delivered by Dr. George Crile, of Cleveland, Chairman of the Board of Regents. His subject will be "The American College of Surgeons—Past, Present and Future."

On Tuesday, Wednesday and Thursday evenings scientific sessions will be held in the Auditorium of the Veterans' Building at which eminent surgeons of the United States and Canada, together with visiting surgeons from foreign countries, will present and discuss papers on surgical subjects of timely importance.

At the annual convocation, to be held in the War Memorial Opera House on Friday evening, the 1935 class of candidates will be received into Fellowship. The president, Dr. Donald C. Balfour, will deliver his inaugural address on this occasion, and the Fellowship address will be delivered by Robert Gordon Sproul, B.S., LL.D., president of the University of California.

HOSPITAL CONFERENCE

The eighteenth annual hospital standardization conference will open with a session in the Gold Ballroom of the Fairmont Hotel at 9:30 on Monday morning at which addresses will be delivered

by distinguished representatives of several organizations. At this session the annual report of the hospital standardization activities of the College for 1935, including the list of approved hospitals, will be presented.

Monday afternoon will be given over to a discussion of hospital problems from various aspects in which administrators, surgeons and others will participate.

Tuesday morning will be devoted to a "panel" discussion of the hospital's obligation to its community and its part in the community life professionally and economically.

A joint session with the Association of Record Librarians will be held on Wednesday morning at which problems concerning hospital records are to be discussed.

Tuesday and Wednesday afternoons will be devoted to definitely planned departmental demonstrations in hospital administration in certain of the San Francisco hospitals. These demonstrations will show how various departments function, affording those present an excellent opportunity to see how other institutions carry on their activities.

Thursday will be Oakland Hospital Day and a program of demonstrations of special interest will be carried on in four of the major hospitals in Alameda County with the co-operation of the Oakland Hospital Council. Many new features and procedures in hospital management will be demonstrated.

Through the courtesy of Dr. D. W. Black, medical director of the Highland Hospital and director of Alameda County health activities, those who are interested in the Alameda plan for medical and hospital care will be given an opportunity to make an excursion through the county on Friday.

FRACTURE CONFERENCE

A conference on fractures will be held under the auspices of the College Committee on the Treatment of Fractures on Tuesday afternoon at 2 o'clock in the Gold Ballroom of the Fairmont Hotel. The chairman's report will include a summary of the activities of the Committee and the accomplishments of its regional committees throughout the United States and Canada. Papers are to be presented as follows:

FREDERIC W. BANCROFT, M.D., New York, Chairman of Committee on Treatment of Fractures, presiding.
Highway First Aid Stations. E. PAYNE PALMER, M.D., Phoenix, Arizona.
Fender Fractures into the Knee Joint. FREDERIC J. COTTON, M.D., Boston.
Status of Fractures in the Field of Surgery. CLAY RAY MURRAY, M.D., New York.
Local Anesthesia in Fractures. E. DUNBAR NEWELL, M.D. Chattanooga, Tenn.
The Causes of Non-Union; Bone Growth and Regeneration. WILLIAM R. CUBBINS, M.D., Chicago.

CANCER SYMPOSIUM

The symposium on cancer, under the auspices of the College Committee on the Treatment of Malignant Diseases, will be held on Thursday afternoon in the Gold Ballroom of the Fairmont Hotel following the annual meeting of the Fellows. The symposium will concentrate on the standard accepted methods for the treatment of cancer.

A report on five-year results of therapy, compiled by the Department of Clinical Research continuing the gathering of statistics on this subject from clinicians in various parts of the United States and Canada during the past several years, will be included.

CHARLES A. DUKES, M.D., Oakland, Calif., Chairman of Committee on the Treatment of Malignant Diseases, presiding.
Prostate. BENJAMIN S. BARRINGER, M.D., New York.
Fundus Uteri. ALSON R. KILGORE, M.D., San Francisco.
Colon. THOMAS E. JONES, M.D., Cleveland.
Larynx. GORDON B. NEW, M.D., and F. A. FIGI, M.D., Rochester, Minn.
Melanoma. FRANK E. ADAIR, M.D., New York.
A Diagnostic Cancer Clinic in a Private Hospital. C. HIRAM WEAVER, M.D., Los Angeles.
Five-Year Results of Treatment. BOWMAN C. CROWELL, M.D., Chicago.

CONFERENCE ON INDUSTRIAL MEDICINE AND TRAUMATIC SURGERY

The Board on Industrial Medicine and Traumatic Surgery will hold its annual conference on Friday afternoon at 2 o'clock in the Gold Ballroom of the Fairmont Hotel. The program includes a report on the activities of the College in conducting investigations and surveys among industrial establishments during the past year in continuation of the work done along these lines during the past five years.

FREDERIC A. BESLEY, M.D., Waukegan, Ill., Chairman of Board on Industrial Medicine and Traumatic Surgery, presiding.
Silicosis and Its Control. R. R. SAYERS, M.D., and R. R. JONES, M.D., Washington.
Analysis of Five Hundred Intra-ocular Steel Operations. SYDNEY WALKER, JR., M.D., Chicago.
Tannic Acid and Silver Nitrate in Burns. ADALBERT BETTMAN, M.D., Chicago.
Heat Exhaustion and Its Prevention. LOYAL A. SHOUDY, M.D., Bethlehem, Pa.
Immediate and Delayed Repair of Tendon Injuries. MICHAEL L. MASON, M.D., Chicago.
Report of the 1935 Survey of Medical Services in Industry by the American College of Surgeons. M. N. NEWQUIST, M.D., Chicago.

OPHTHALMOLOGY AND OTOLARYNGOLOGY

The committee in charge of the section on surgery of the eye, ear, nose and throat has arranged a program of ophthalmological and otolaryngological clinics and demonstrations at the hospitals and medical schools, as published in tentative form in the following pages. Scientific sessions will be held at the Fairmont Hotel on Tuesday, Wednesday, Thursday and Friday mornings, at which papers are to be presented as follows:

Relation of Orthoptics to the Surgical Treatment of Concomitant Strabismus. A. D. PRANGER, M.D., Rochester, Minn.

Title to be announced. CLIFFORD B. WALKER, M.D., Los Angeles.

Surgical Correction of Defects Due to Paralysis of the Muscles of the Eyes or of the Eyelids. MEYER WIENER, M.D., St. Louis.

What the General Public Should Know About the Eye. J. O. MCREYNOLDS, M.D., Dallas, Texas.

A New Iridosclerectomy Operation for Glaucoma. CONRAD BERENS, M.D., New York.

Analysis of Five Hundred Intra-Ocular Steel Operations. SYDNEY WALKER, JR., M.D., Chicago.

Brief Consideration of the History of the Development of Mastoidectomy. ROBERT SONNENSCHEIN, M.D., Chicago.

Title to be announced. F. E. LEJEUNE, M.D., New Orleans.

Cancer of the Larynx. W. E. SAUER, M.D., St. Louis.

Surgical Approach to the Nasal Accessory Sinuses. WILLIAM MITHOEFER, M.D., Cincinnati.

Selection of Treatment for Malignancy of the Upper Respiratory Tract. FREDERICK A. FIGI, M.D., Rochester, Minn.

Unique Symptoms and Effects of Sphenoidal Empyema. CHESTER H. BOWERS, M.D., Los Angeles.

COMMUNITY HEALTH MEETING

Following its established custom and in recognition of its obligation to the public to provide authoritative information on modern surgery, better hospitals, and the prevention of disease, a community health meeting will be held on Wednesday evening at 8 o'clock, under the auspices of the American College of Surgeons, in the Exposition Auditorium, presenting a program appropriate for the occasion and consisting of brief interesting talks on scientific medicine, health, and hospitals, also a motion picture film on a medical subject of interest to the laity.

ANNUAL MEETING

The annual meeting of the Fellows of the College will convene in the Gold Ballroom of the Fairmont Hotel at 2 o'clock Thursday afternoon. Reports by the officers and chairmen of the standing committees on the various activities of the College will be presented, followed by the election of officers.

MEETING OF NEW FELLOWS

Candidates for fellowship in the American College of Surgeons, class of 1935, will assemble in the Gold Ballroom of the Fairmont Hotel at 11 a.m. on Friday for the necessary instructions previous to receiving their fellowships and to sign the fellowship roll.

A VACATION ON THE PACIFIC COAST AND THE CLINICAL CONGRESS

Many Fellows of the College and their guests, who will attend the Clinical Congress in San Francisco in October, are planning to take advantage of the opportunity which naturally suggests itself to include a vacation and sight-seeing trip on the Pacific coast. All the railways are offering very low round-trip rates with liberal stopover privileges from all parts of the United States and Canada, with the added privilege of traveling to the coast by one route and returning by another, thereby affording unusual opportunities for visiting many points of interest en route.

When nature fashioned the Pacific coast she was in a spendthrift mood. From the Canadian border to the Mexican line she scattered her beauties and wonders with a prodigal hand—mountains, rivers, waterfalls, oceans, beaches, forests, lakes; even a live volcano, the only one in the United States.

Few cities have so impressive a setting as San Francisco. The rugged hills upon which it is built, the Golden Gate, Mt. Tamalpais, the misty bay to the east, Oakland and Berkeley, and the hills beyond, all contribute to its grandeur. It is a pleasing picture and the citizens of San Francisco have not been unmindful of it. Their parks and residence districts have a dignity and beauty in keeping with the scene about them.

The glamour of the city is inescapable, but no amount of description can picture accurately this unique city. One must see for himself how the many charming aspects of San Francisco and its environs blend into one delightful and unforgettable picture.

Along the Pacific coast one will find much to claim his attention. First, there is the California-Pacific International Exposition at San Diego—a World's Fair of magnitude, with many important medical and other scientific exhibits—erected in Balboa Park, a tropical fairyland. The buildings, which are permanent structures, have their dignity and beauty enhanced by the gorgeous setting.

Los Angeles with its mountain background, its broad boulevards, its nearby beaches, its hospitality—and Hollywood—afford opportunities for

entertainment and recreation. A one-day trip to enchanting Catalina Island, with its balmy south sea island atmosphere, would naturally suggest itself.

Traveling south but a short distance from San Francisco, one enters the San Joaquin valley at Merced—the gateway to Yosemite National Park, where one views one of the most famous spectacles of nature. The valley occupies but eight square miles, but in this limited space are gathered more natural wonders than can be found in any other similar area in the world. It contains eight waterfalls, the lowest twice the height of Niagara, and the highest the equal of ten Niagaras. There are meadows of deep grass and wild flowers, a rushing mountain river, forests and towering cliffs. A short distance beyond is Sequoia National Park, containing thousands of giant Sequoia, the largest and oldest living things on the face of the globe.

Del Monte and Pebble Beach, on the famous seventeen mile drive, are but a short distance from San Francisco. Other nearby points of interest are Paso Robles, with its almond groves, lovely Santa Barbara with its famous Old Mission, and a score of cities whose names are associated with the romantic Spanish period—a fairyland of natural and cultivated beauty.

To the north there are many cities to claim your attention: Vancouver, in British Columbia, built up against mighty mountains with a primeval forest almost at its environs; Seattle, the great shipping center of the northwest, with Puget Sound to the west and beyond it the white-capped Olympics; in the distance the Cascade Mountains and looming to the southeast, Mt. Rainier, held in special veneration by the Indians as "the mountain that was God"—no peak in the United States is so majestic; Portland, famous for its natural beauty—a literal bower of roses; the blue miracle of Crater Lake, Mt. Shasta and Lassen Peak, the only active volcano in the United States.

Traveling through the mountains one will enjoy the grandeur of the high Sierras, and a visit en route to the Mormon capitol—Salt Lake City—will be a notable feature of the journey.

No matter what route one takes he will view a truly great and inspiring American scene—the thriving farm lands of the midwest, the noble stretches of prairie, the sublime mountain ranges of the Rockies, the grandeur of the desert, the towering forests of the far west, and then the blue Pacific.

This year one will travel in comfort and luxury undreamed of a short time ago. Whatever route one travels he will find his train air-conditioned. This single factor adds so much to the comfort and pleasure of a transcontinental journey that it definitely and certainly marks the beginning of a new era in transportation history.

RAILWAY FARES FROM VARIOUS CITIES TO SAN FRANCISCO AND RETURN

Low round-trip fares will be in effect from all points in the United States and Canada. Consult your local ticket agent as to exact fare. Summer tourist tickets are good going via one route and returning via the same or any other authorized route, with a final return limit of November 30.

	Round Trip Fare	Lower Berth One Way
Atlanta	$100.75	$21.25
Baltimore	120.75	24.00
Boston	132.80	25.88
Buffalo	109.55	21.38
Chicago	86.00	15.75
Cincinnati	97.00	19.50
Cleveland	101.35	19.50
Detroit	98.30	19.50
Duluth	86.00	17.75
Kansas City	72.00	13.25
Memphis	85.15	14.50
Minneapolis	86.00	15.75
Montreal	122.55	24.75
New York	126.90	24.75
New Orleans	85.15	14.00
Omaha	72.00	13.25
Philadelphia	122.85	24.00
Pittsburgh	107.10	20.25
Portland, Ore	29.70	5.50
St. Louis	81.50	15.00
St. Paul	86.00	15.75
Seattle	37.05	6.75
Toronto	108.15	21.38
Vancouver, B. C	42.55	8.75
Washington	120.75	24.00
Winnipeg (via Portland)	86.00	18.75

ADVANCE REGISTRATION

The hospitals and medical schools of San Francisco and Oakland afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will

be limited to the capacity of the room in which that clinic will be given.

A registration fee of $5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Fairmont and Mark Hopkins hotels. At the former the Terrace Ballroom and Foyer, the Gold Ballroom and other large rooms on the main floor and on the terrace have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, exhibits, executive offices, etc. The Peacock Court and Room of the Dons at the Mark Hopkins will be utilized for various scientific sessions.

The Technical Exhibition, including the registration and clinic ticket bureaus, will be located in the ballroom and foyer on the terrace floor of the Fairmont Hotel. In these rooms will also be found the bulletin boards on which the daily clinical program will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

SAN FRANCISCO HOTELS AND THEIR RATES

In addition to the two headquarters hotels—the Fairmont and Mark Hopkins—there are a number of first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. The following hotels are recommended by the Committee:

	Minimum Rate with Bath	
	Single	Double
Bellevue, Geary and Taylor	$3.00	$4.00
Californian, Taylor and O'Farrell	3.00	4.50
Clift, Geary and Taylor	3.50	5.00
El Cortez, Geary near Taylor	3.00	4.50
Fairmont, Mason and California	3.50	5.00
Gaylord, Jones near Geary	3.00	4.00
Mark Hopkins, Mason and California	3.50	5.00
Palace, Market and New Montgomery	3.50	5.00
Plaza, Post and Stockton	3.00	4.00
Sir Francis Drake, Powell and Sutter	3.50	5.00
Stewart, 353 Geary	2.50	4.00
St. Francis, Union Square	3.50	5.00

ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

Monday, 9:30–12:30—Gold Ballroom, Fairmont Hotel

ROBERT B. GREENOUGH, M.D., Boston, presiding.

Greetings. JACOB C. GEIGER, M.D., and LEON M. WILBOR, M.D., San Francisco.

Introduction of distinguished guests.

The Hospital Standardization Movement of the American College of Surgeons and Announcement of Approved List of Hospitals for 1935. GEORGE CRILE, M.D., Cleveland.

The Hospital and the Changing Social Order. SISTER JOHN GABRIEL, R.N., Seattle, Wash.

Opportunities for the Training of Surgeons in the Approved Hospital. IRVIN ABEL, M.D., Louisville.

Organization and Administration of an Oxygen Therapy Service in a General Hospital. R. C. BUERKI, M.D., Madison, Wis.

An Accredited Pathologist for Every Approved Hospital. PHILIP HILLKOWITZ, M.D., Denver.

The Future of the Voluntary Hospital. ROBERT JOLLY, Houston, Texas.

Discussion. FREDERIC A. BESLEY, M.D., Waukegan, Ill.

Monday, 2:00–5:00—Gold Ballroom, Fairmont Hotel

BENJAMIN W. BLACK, M.D., Oakland, presiding.

Application of the Principles of Hospital Standardization from the Viewpoints of:

Hospital Trustee. W. C. CRANDALL, La Jolla, Calif.

Hospital Administrator. PAUL H. FESLER, Chicago.

Medical Staff Member. JACOB F. HIGHSMITH, M.D., Fayetteville, N.C.

Clinical Pathologist. ALVIN G. FORD, M.D., Pasadena, Calif.

Radiologist. EDWARD S. BLAINE, M.D., Los Angeles.

Nurse. SISTER MARY STEPHANIE, R.N., San Francisco.

Dietitian. LUCILE WAITE, San Leandro, Calif.

Medical Social Worker. MARGUERITE L. SPIERS, Oakland.

Medical Educator. ALEXANDER R. MUNROE, M.D., Edmonton, Alta.

Economist. DANIEL CROSBY, M.D., Oakland.

Tuesday, 9:30–12:30—Gold Ballroom, Fairmont Hotel

ARTHUR M. CALVIN, St. Paul, presiding.

Innovations in Hospital Equipment and Supplies from the Standpoint of Efficiency, Economy, and Service. G. W. OLSON, Los Angeles.

The Institutional Care of Chronic and Convalescent Patients. A. C. JENSEN, San Leandro, Calif.

Panel Discussion Conducted by JOSEPH G. NORBY, Minneapolis.

To Create Understanding—Public Relations. FRANK J. WALTER, Denver.

To Provide Adequate Service. G. WAITE CURTIS, San Francisco.

To Bring the Cost of Hospital Service Within Reach of the People Served. R. E. HEERMAN, Los Angeles.

To Provide Adequate Service to the Indigent Patient. J. V. BUCK, Spokane Wash.

To Educate Nurses, Doctors, and Others Engaged in the Care of the Sick. CAROLYN E. DAVIS, Portland, Ore.

Tuesday, 2:00–5:00—St. Mary's Hospital

Demonstrations and round table discussions dealing with methods of standardization and administration. Conducted by SISTER MARY THOMASINE, Superintendent, and heads of departments.

Business administration—equipment, personnel, accounting, reports, hospital costs, methods for meeting present economic conditions.

Organization and management of food service—control and responsibility, personnel, types of service, special diets.

Pharmacy service—organization and management, physical requirements, personnel, accounting.

Adjunct departments—Organization and management of clinical laboratory, X-ray and physical therapy departments, technical service, routine examination, records and filing.

Tuesday, 8:00–10:00 p.m.—St. Mary's Hospital

Round Table Conference—A discussion of every-day hospital problems as applied to the professional and economic aspects of hospital administration. Conducted by ROBERT JOLLY, Houston, Texas.

Wednesday, 9:30–12:30—Gold Ballroom, Fairmont Hotel

Joint Session with Association of Record Librarians of North America. R. C. BUERKI, M.D., Madison, Wis., presiding.

Securing, Supervising, and Using Medical Records. MALCOLM T. MACEACHERN, M.D., Chicago.

Discussion from the viewpoints of:

Hospital Administrator. THEODORE E. SWARTZ, M.D., Oakland.

Physician. S. MARX WHITE, M.D., Minneapolis.

Surgeon. ALTON OCHSNER, M.D., New Orleans.

Obstetrician. D. G. TOLLEFSON, M.D., Los Angeles.

Ophthalmologist and Otolaryngologist. WILLIAM W. PEARSON, M.D., Des Moines, Iowa.

Record Librarian. MINNIE G. HILL, Los Angeles.

Group Studies Essential to Scientific Efficiency. SISTER M. SERVATIA, R.N., Kansas City, Mo.

Wednesday, 2:00–5:00—University of California Hospital

Demonstration and round table conference on the organization and management of the medical records department. Conducted by F. S. DURIE, Superintendent and heads of departments.

Physical requirements, personnel, supervision, filing and cross-indexing records, uses of records, special problems, standard nomenclature.

Wednesday, 2:00–5:00—San Francisco Hospital

Demonstrations and round table conference on care of the obstetrical patient in the general hospital. Conducted by LEON M. WILBOR, M.D., Superintendent, and heads of departments.

Prenatal care, admission procedure, care of the patient in labor, delivery room technique, postpartum care, the isolated or septic patient, care of the newborn, follow-up and end results, review of morbidities and mortalities, records. Motion picture "Around the Clock with You and Your Baby."

OAKLAND HOSPITAL DAY—THURSDAY

10:00 a.m.–1:00 p.m.—Providence Hospital

Demonstrations and round table conferences:

Economies in hospital management. Staff of Providence Hospital.

Organization and management of the housekeeping department. Staff of Fairmont Hospital.

Organization and functioning of the social service department. Staffs of Alameda County and Berkeley General Hospitals.

2:00–5:00—Samuel Merritt Hospital

Demonstrations and round table conferences:

Admission and discharge procedures. Staffs of the Samuel Merritt and Peralta Hospitals.

Organization and management of a central supply room. Staff of Samuel Merritt Hospital.

Hospital formulary. Staff of Peralta Hospital.

Friday, 10 a.m.

Inspection of the emergency system of the Alameda County Hospital and tour of county institutions for study of the Alameda plan.

PRELIMINARY PROGRAM FOR EVENING MEETINGS

Presidential Meeting—Monday, 8:15 p.m.—War Memorial Opera House

Address of Welcome. HOWARD C. NAFFZIGER, M.D., San Francisco, Chairman of Committee on Arrangements.

Introduction of Foreign Guests.

Address of the President: The Conscience of the Surgeon. ROBERT B. GREENOUGH, M.D., Boston.

Inauguration of Officers: President, DONALD C. BALFOUR, M.D., Rochester, Minn.; First Vice-President, ARTHUR W. ALLEN, M.D., Boston; Second Vice-President, JOHN A. GUNN, M.D., Winnipeg.

Annual Oration on Surgery: The American College of Surgeons—Past, Present and Future. GEORGE CRILE, M.D., Cleveland.

Tuesday, 8:15 p.m.—Auditorium, Veterans Building

Symposium on Hypertension:

Medical Aspect. S. MARX WHITE, M.D., Minneapolis.

General Neurological Procedures. ALFRED W. ADSON, M.D., Rochester, Minn.

Neurological Treatment. MAX MINOR PEET, M.D., Ann Arbor, Mich.

Wednesday, 8:15 p.m.—Auditorium, Veterans Building

The Diagnosis and Treatment of Stone in the Common Duct. ARTHUR W. ALLEN, M.D., Boston.

Adrenal Cortical Tumors. GEORGE F. CAHILL, M.D., New York.

Fracture Oration: Fundamentals versus Gadgets in the Treatment of Fractures. PAUL B. MAGNUSON, M.D., Chicago.

Thursday, 8:15 p.m.—Auditorium, Veterans Building

Ischemic Contractures. ARTHUR STEINDLER, M.D., Iowa City, Iowa.

Cerebral Injuries Due to External Trauma. GEORGE W. SWIFT, M.D., Seattle.

The Diagnosis of Endometrial Hyperplasia. LUCIUS E. BURCH, M.D., Nashville, Tenn.

Treatment of Peptic Ulcer, Based on Physiological Principles. ALTON OCHSNER, M.D., New Orleans.

Convocation—Friday, 8:15 p.m.—War Memorial Opera House

Invocation.

Presentation of Candidates for Fellowship.

Conferring of Fellowships. The President.

Conferring of Honorary Fellowships. The President.

Presidential Address. DONALD C. BALFOUR, M.D., Rochester, Minn.

Fellowship Address: The Social Significance of Medicine. ROBERT GORDON SPROUL, B.S., LL.D., Berkeley, Calif.

COMMITTEE ON ARRANGEMENTS

Executive Committee

Howard C. Naffziger, Chairman; Thomas F. Mullen, Secretary

Leroy C. Abbott
Harold Brunn
Edmund Butler
Whitfield Crane
Charles A. Dukes
Leo Eloesser
Philip K. Gilman
Oliver D. Hamlin
Frank Hinman
Emile F. Holman
Alson R. Kilgore
Frank W. Lynch
Joseph L. McCool
Isaac W. Thorne

SUB-COMMITTEES—SAN FRANCISCO

Clinical Program Committee (General Surgery)—Alson R. Kilgore, Chairman; Edmund Butler, Thomas F. Mullen.

Clinical Program Committee (Eye, Ear, Nose and Throat Surgery)—Joseph L. McCool, Chairman; H. B. Graham, Warren D. Horner.

Transportation Committee—Emile F. Holman, Chairman; G. D. Delprat, Millard R. Ottinger.

Public Meeting Committee—Jacob C. Geiger, Chairman; Harold M. Behneman, Edgar L. Gilcreest, Jacques P. Gray, Leon Wilbor.

Golf Committee—Leroy Brooks, Chairman; Harry Alderson, James Morgan, Frank Sheehy.

HOSPITAL REPRESENTATIVES

SAN FRANCISCO—GENERAL SURGERY

Franklin Hospital—Ernst Gehrels, Leroy Brooks.

French Hospital—Asa Collins, Edmund Morrissey.

Hospital for Children—Leroy Abbott, Alma Pennington.

Letterman General Hospital—R. F. Metcalfe.

Mary's Help Hospital—Isaac Thorne, Raymond Millzner, Everett Carlson, Dudley Smith.

Mount Zion Hospital—Harold Brunn, Franklin Harris, Albert L. Brown.

St. Francis Hospital—James O'Connor, Calvin A. Walker.

St. Joseph's Hospital—Alson R. Kilgore, J. Minton Meherin.

St. Luke's Hospital—G. D. Delprat, Otto Pflueger.

St. Mary's Hospital—Thomas E. Bailly, Philip Arnot, Daniel Sooy.

San Francisco Hospital—Stanford University Service: Leo Eloesser, H. Matthewson, L. Rogers. University of California Service: Harold Brunn, C. Latimer Callander, George K. Rhodes.

Shriners' Hospital for Crippled Children—Sylvan Haas.

Southern Pacific General Hospital—William Washburn, Frank R. Girard.

Stanford University Hospitals—Emile Holman, Philip K. Gilman, Frederick Reichert.

Stanford University School of Medicine—Loren Chandler, Emmet Rixford.

United States Marine Hospital—Mark J. White, Richey L. Waugh.

University of California Hospitals—Howard C. Naffziger, H. Glenn Bell.

University of California Medical School—Langley Porter, Wallace Terry.

Veterans Administration Hospital—P. E. Johnson, Berthel H. Henning, John A. Kennedy.

SAN FRANCISCO—SURGERY OF THE EYE, EAR, NOSE AND THROAT

French Hospital—Edward C. Fabre-Rajotte, Victor d'Ercole.

Hospital for Children—George Hosford.

Letterman General Hospital—A. E. Schlanser, H. C. Maxwell.

Mary's Help Hospital—Frank Hand, J. W. Crawford.

Mount Zion Hospital—Frank Rodin, Herbert Cohn.

St. Francis Hospital—Constantine Bricca, Aubrey Rawlins.

St. Joseph's Hospital—Roy Parkinson.

St. Luke's Hospital—Ambrose E. Edgerton, Charles Bates.

St. Mary's Hospital—Francis Conlan, Stanley Burns.

Southern Pacific General Hospital—Wilbur Swett.

Stanford University Hospitals—Edward Sewell, Hans Barkan, Harrington Graham, Louis Morrison.

United States Marine Hospital—Rae Ashley.

University of California Hospitals—Wallace Smith, Fred C. Cordes, Robert C. Martin, C. Allen Dickey.

Veterans Administration Hospital—J. J. Caviness, Otto Barkan.

OAKLAND EXECUTIVE COMMITTEE

Oliver D. Hamlin, Chairman

Charles A. Dukes, Vice Chairman

Whitfield Crane, Secretary

Clinical Program Committee—Lemuel P. Adams, Warren B. Allen, Harry H. Appledorn, Frank S. Baxter, Julian J. Benton, Whitfield Crane, Charles A. Dukes, Sumner Everingham, Channing Hall, Oliver D. Hamlin, Henry W. Harding, Harold H. Hitchcock, T. O. Lake, Theodore C. Lawson, Ergo Majors, W. Earl Mitchell, George McClure, Albert Meads, Raymond J. Nutting, Clair Rasor, Dextor N. Richards, Milton H. Shutes, H. R. Smithies, Clifford Sweet, Frank Walsh, Don D. Weaver.

PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY, SURGICAL PATHOLOGY, ETC.

OPERATIVE CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

SAN FRANCISCO HOSPITAL

University of California Service

HAROLD BRUNN, GEORGE K. RHODES, A. R. KILGORE, C. L. CALLANDER, S. H. MENTZER, A. L. BROWN, H. W. STEPHENS, F. S. FOOTE, M. W. DEBENHAM, H. M. BLACKFIELD and L. GOLDMAN. General surgery.

F. HINMAN, C. JOHNSON, S. OLSEN, L. PLAYER, J. J. SULLIVAN, W. A. CARROLL and T. O. POWELL. Urological operations.

W. G. MOORE, A. M. VOLLMER and M. SCHULZE. Gynecological operations.

H. W. FLEMING, H. A. BROWN and L. B. LAWRENCE. Neurosurgical operations.

LEROY ABBOTT, F. G. LINDE, F. C. BOST, W. J. COX and K. O. HALDEMAN. Orthopedic operations.

Stanford University Service

LEO ELOESSER. Lobectomy for lung tumor; flap operation for tuberculous empyema; disarticulation at knee joint.

W. L. ROGERS. Apicolysis (paraffin fill).

J. M. MEHERIN. Gastric resection (Billroth I).

EDMUND BUTLER. Pyloroplasty for peptic ulcer; atresia of colon, congenital.

J. CLINE. Exploration of biliary duct.

C. MATHEWSON. Open reduction of spiral fracture of the tibia; sequestrectomy for tuberculosis of the pelvis.

D. KING. Nonunion of carpal scaphoid.

M. R. OTTINGER. Resection for carcinoma of the colon.

E. TOWNE. Laminectomy for decompression of cauda equina.

E. MORRISSEY. Removal of cord tumor.

L. REYNOLDS. Cystectomy for carcinoma of the bladder.

G. HARTMAN. Suprapubic prostatectomy.

L. MICHAELSON. Plastic on kidney pelvis.

R. CRAIG. Nephrectomy.

K. SCHAUPP. Removal of fibromyoma of the uterus.

A. PETTIT. Vesicovaginal fistula.

H. VON GELDERN. Perineal repair operation.

C. COOLEY. Operation for pelvic inflammatory disease.

R. DUNN. Hyam's conization of the cervix.

D. DALLAS. Vaginal hysterectomy.

UNIVERSITY OF CALIFORNIA HOSPITAL

HOWARD C. NAFFZIGER, D. JONES, JR., H. BROWN and R AIRD. Neurosurgical operations.

HAROLD BRUNN and H. STEPHENS. Thoracic surgery.

R. ABBOTT, F. BOST, K. HALDEMAN and W. KEYS. Orthopedic surgery.

FRANK W. LYNCH, A. MAXWELL, M. SCHULTZE, D. MORTON and C. HAYDEN. Gynecological ar l obstetrical operations.

FRANK HINMAN, C. JOHNSON, S. OLSEN and B. WAYMAN. Urological operations.

W. S. TERRY. General surgical operations; thyroidectomy.

H. SEARLS and H. GLENN BELL. Carcinoma of colon; cholecystectomy; popliteal aneurism.

C. ROSSEN. Appendectomy; hernioplasty.

M. S. WOOLF. Carcinoma of rectum and lower bowel.

F. FOOTE. Partial obstruction, new operations.

E. O. BARTLETT. Carcinoma of breast.

STANFORD UNIVERSITY HOSPITAL

EMMET RIXFORD, EDMUND BUTLER, R. GILMAN, L. CHANDLER, EMILE HOLMAN and S. BUNNELL. General abdominal surgery; gastro-intestinal surgery; hernias.

EMILE HOLMAN and LEO ELOESSER. Thoracic surgery.

F. REICHERT and E. TOWNE. Neurosurgical operations.

R. GILMAN, EMMET RIXFORD and EMILE HOLMAN. Thyroid, biliary tract, liver and pancreas surgery.

A. L. FISHER, D. KING and M. MENSOR. Orthopedic operations.

J. DILLON and L. REYNOLDS. Urological operations.

L. EMGE, H. A. STEPHENSON, C. FLEUHMANN, P. E. HOFFMAN, G. CRAIG and W. STEVENS. Gynecological and obstetrical operations.

F. REICHERT and EMILE HOLMAN. Cardiac conditions, circulatory diseases.

C. B. PALMER and R. BURROWS. Injections, anesthesia.

R. A. SCARBOROUGH. Proctological operations.

A. DAVIS and S. BUNNELL. Plastic surgery; industrial cases; skin diseases.

ST. MARY'S HOSPITAL

T. E. BAILLY. Gastric surgery; gastrectomy.

RODNEY YOELL. Gall-bladder surgery; cholecystectomy.

D. SOOY. Surgical intervention for duodenal ulcer.

C. P. MATHE. Nephropexy for nephroptosis.

E. TOPHAM. Inguinal hernia.

JUSTIN MCCARTHY. Industrial emergency cases.

EDMUND BUTLER. Surgery of the colon.

GEORGE K. RHODES. Emergency surgery.

EDMUND MORRISSEY. Sympathectomy for Raynaud's disease.

PHILIP ARNOT. Obstetrical surgery.

T. GIBSON. Nephrectomy.

W. FAULKNER. Bronchoscopic diagnosis in cases of lung abscess.

J. LOUTZENHEISER. Orr treatment for delayed bony union.

LETTERMAN GENERAL HOSPITAL

R. F. METCALFE. Cauterization of cervix; perineorrhaphy; suspension of uterus; gastrojejunostomy; cholecystectomy; hemorrhoidectomy; colostomy for rectal carcinoma; cesarean section.

F. L. COLE. Hernia; appendectomy; inguinal hernia; ventral hernia.

H. S. BLESSE. Genito-urinary operations; electrical resection.

B. S. BURNET. Thoracotomy for empyema; orthopedic operations; bone graft; open reduction of tibia; excision of cartilage, knee.

P. E. DUGGINS. Curettage and insertion of Carsten pessary for sterility.

ST. JOSEPH'S HOSPITAL

ALSON R. KILGORE, J. M. MEHERIN, F. SHEEHY and C. E. SMITH. General surgical operations.

R. SOTO-HALL and K. HALDEMAN. Orthopedic operations

E. MORRISSEY. Neurosurgical operations.

H. VON GELDERN. Gynecological operations.

T. GIBSON. Urological operations.

MOUNT ZION HOSPITAL

HAROLD BRUNN. Total thyroidectomy for cardiac disease.
F. I. HARRIS. Torek operation for undescended testicle, first and second stage procedures; resection for lesions of descending colon; radical mastectomy, Percy cautery and endotherm.
A. L. BROWN. Plastic repair of pendulous breasts; herniotomy.
W. WALDEYER. Appendectomy.
M. GROPER and A. WHITE. Blood transfusion, citrate, Linderman and Unger methods.
L. HOFFMAN. Hysterectomy.
L. D. PRINCE, A. SIRBU and DAVID CHARMAK. Radical clavectomy; fracture of os calcis.
H. BLACKFIELD. Plastic correction of congenitally protruding ears.
HAROLD BRUNN and A. L. BROWN. Phrenic avulsion; thoracoplasty.
A. ZOBEL and D. A. SUSNOW. Electrocoagulation of tumors of the rectum; hemorrhoidectomy under local infiltration.
L. C. JACOBS. Calculi of the urinary bladder; transurethral prostatectomy.
H. A. R. KREUTZMANN. The problem of urinary lithiasis; nephrotomy; pyelotomy; nephrectomy.
B. STRAUSS and M. POLSE. Hydrocele operation; plastic operation for phimosis; cystoscopy.
A. EPSTEEN. Injection of vas deferens for chronic epididymitis.
R. K. SMITH. Classical cesarean section.
A. BERNSTEIN. Demonstration of cervical repair immediately following delivery.
F. PEARL. Muscle splitting extraperitoneal lumbar sympathetic ganglionectomy, a new approach; muscle splitting posterior cervicodorsal sympathetic ganglionectomy.
EDWARD H. BOLZE, HERBERT H. SCHULTZ and DR. LAZAR. Demonstration of introduction of anesthesia by avertin, evipal, gas and oxygen, spinal.

SOUTHERN PACIFIC HOSPITAL

W. B. COFFEY and J. D. HUMBER. Superior cervical sympathectomy for angina pectoris, moving picture demonstration in natural color.
C. MATHE and T. GIBSON. Transurethral prostatectomy.
E. GREENWOOD. Cholecystectomy.
F. R. GIRARD. Inguinal hernia; ambulant treatment by injection.
C. WALKER and J. BOHM. Open reduction of fractures.
OSCAR F. NOLAN and THOMAS E. GIBSON. Suprapubic prostatectomy.
W. W. WASHBURN. Thyroid surgery.

FRENCH HOSPITAL

F. A. LOWE. Fractured humerus; internal derangements of knee joint.
G. W. PIERCE and G. O'CONNOR. Removal of nasal hump.

VETERANS ADMINISTRATION

Staff. Coffey operation for carcinoma of the rectosigmoid, second state; gastrectomy.

ST. LUKE'S HOSPITAL

ALANSON WEEKS, G. D. DELPRAT, PAUL CASTELHUN, A. H. ROSBURG, OTTO H. PFLUEGER, DR. SULLIVAN, DR. MOORE and ALBERT M. VOLLMER. General surgical operations.
GEORGE J. MCCHESNEY, RUDOLPH L. DRESEL and DR. COX. Orthopedic operations.
L. P. PLAYER, HERBERT D. CRALL and MILEY B. WESSON. Urological operations.
J. M. MORGAN. Proctological operations.

U. S. MARINE HOSPITAL

ROBERT A. JONES. Excision of pilonidal sinus and rectal operations; cholecystectomy and autoplasty (Gillies tubular flap); Dupuytren's contracture.
RICHEY L. WAUGH. Inguinal hernioplasty using pedicled fascial strips; operation for sciatica (Heyman); arthrotomy of the knee with excision of internal semilunar cartilage; bunion operation (Peabody); phrenic neurectomy.
FLETCHER C. STEWART. Transurethral resection of prostate.

FRANKLIN HOSPITAL

E. GEHRELS. Gastro-intestinal surgery.
L. BROOKS. Abdominal operations.
J. SALE, V. DILLON, W. MONTGOMERY and W. COX. Industrial surgery and orthopedics.
G. W. PIERCE and G. O'CONNOR. Reconstruction surgery of hand, face and neck after burns; repair of eyelids; correction of flexion contractures.

MARY'S HELP HOSPITAL

R. MILLZNER. Radical neck dissection.
E. CARLSON and C. C. MCCRAE. Abdominal operations.
M. MENSOR and L. PARKER. Orthopedic surgery.
M. VECKI. Urological operations.
H. VON GELDERN and A. SCHMIDT. Gynecological and obstetrical operations.

HOSPITAL FOR CHILDREN

C. HOAG. Thyroidectomy.
MURIEL E. EDWARDS. Thyroglossal duct cyst.
ALMA PENNINGTON. Supravaginal hysterectomy; total hysterectomy; vaginal plastic.

ST. FRANCIS HOSPITAL

G. B. O'CONNOR. Plastic surgery; Reconstruction of face after burns; rib cartilage transplant to the nose; removal of nasal hump; cleft palate; reconstruction surgery of the hand.
W. W. WASHBURN. Thyroidectomy.
L. R. REYNOLDS and O. NOLAN. Prostatectomy, ureteral transplants.

SHRINER'S HOSPITAL

SYLVAN L. HAAS. Longitudinal osteotomy; transplantation of muscles in paralysis; stabilization of foot; fusion of spine; lengthening of leg; congenital dislocation of hip; Sever operation for obstetrical paralysis with transplantation of teres major; fusion of hip; plastic operation.

CLINICAL DEMONSTRATIONS IN SAN FRANCISCO HOSPITALS—DAILY

GENERAL SURGERY

A. S. WHITE and F. I. HARRIS. Injection treatment of hernia.

HAROLD BRUNN. Appendicitis.

S. R. SHERMAN. Rupture of the spleen.

J. HOMER WOOLSEY and H. GLENN BELL. Splenectomy.

WALTER B. COFFEY. Inspection of an industrial medical and surgical center; ward rounds; demonstration of cases; postoperative treatment.

EMMET RIXFORD. Knotty problems in industrial surgery: Traumatic carcinoma of breast; ruptured heart; traumatic thrombosis of iliac and other large veins.

EMILE HOLMAN. Operative cure of recurrent and direct inguinal hernia.

GEORGE K. RHODES. Hematogenous perinephric abscess; peritonitis and drainage.

M. W. DEBENHAM. Aseptic meningitis following spinal anesthesia.

A. L. BROWN. Pulmonary embolectomy, motion picture demonstration of the Trendelenburg operation on cadaver.

H. BRODIE STEPHENS. Subphrenic abscess; vaccination of the pleural and abdominal cavities.

WALTER BIRNBAUM. Tendon repair; acute gonococcic tenosynovitis.

ALSON R. KILGORE, OTTO H. PFLUEGER and R. S. STONE. Treatment of breast cancer, end results.

OTTO H. PFLUEGER. Soft tissue sarcomas.

ALSON R. KILGORE. Cystic disease of the breast; cancer.

C. L. CALLANDER. Gas bacillus infection; new amputation of thigh in lower third; treatment of septic joints.

EDMUND BUTLER. Emergency surgery.

EDMUND BUTLER, L. R. REYNOLDS, L. H. GARLAND and J. B. MCNAUGHT. Old healed ruptured bladders, diagnostic difficulties and value of X-ray in diagnosis; X-ray in differential diagnosis of acute abdomen.

EUGENE S. KILGORE. Circulatory disease in differential diagnosis of acute abdomen.

CARLETON MATHEWSON, JR., and J. B. MCNAUGHT. Lymphogranuloma inguinale.

A. S. MUSANTE. Postoperative infections.

I. W. THORNE. Squamous and basal cell carcinoma of face and neck, pathology, diagnosis and treatment.

Z. E. BOTIN. Biopsies and tumor surgery; mixed tumors of the parotid.

EVERETT CARLSON. Carotid body tumors; splenectomy, indications and technique.

FRANK E. STILES. Treatment of varicose veins.

J. F. RICKARD. Intestinal obstruction.

SURGERY OF THE THYROID

WILLIAM J. KERR, HENRY H. SEARLS, JANE T. PAXSON and R. S. STONE. Activities of the thyroid committee of the University of California Hospital with follow-up studies after various lines of treatment.

HENRY H. SEARLS, E. I. BARTLETT and C. L. CONNOR. Chronic diffuse thyroiditis.

HENRY H. SEARLS and JANE T. PAXSON. Clinical picture of toxic adenoma with normal or lowered metabolic rate.

WILLIAM J. KERR. The heart in hyperthyroidism.

M. L. MONTGOMERY. Lingual thyroid.

THEODORE ALTHAUSEN. Surgical implications of hepatic damage in thyrotoxicosis.

R. J. MILLZNER. Parathyroid damage during thyroidectomy.

GENITO-URINARY SURGERY

FRANK HINMAN, CLARK M. JOHNSON and BRENT WEYMAN. Tumors of the testicle, pathology, demonstration of hormone tests, end-results; uretero-intestinal anastomosis, experimental work, drawings and motion picture demonstration, demonstration of patients; prostatism, pathology, indications for different types of surgery, end-results by different methods.

C. P. MATHE. Surgery of the prostate.

T. E. GIBSON. Newer aspects of renal tuberculosis.

L. P. PLAYER and H. D. CRALL. Gracilis transplantation for urinary incontinence.

MILEY B. WESSON. Conservative surgical treatment of nephrolithiasis.

L. C. JACOBS. Calculi of urinary bladder; suprapubic and transurethral prostatectomy.

H. A. R. KREUTZMANN. Urinary lithiasis, nephrotomy, pyelotomy and nephrectomy.

BERNARD STRAUSS and M. L. POLSE. Operation for hydrocele; plastic operation for phimosis.

A. EPSTEEN. Injection of vas deferens for chronic epididymitis.

J. V. LEONARD and GEORGE W. HARTMAN. Demonstration in urology.

C. P. MATHE and T. E. GIBSON. Transurethral prostatectomy.

T. E. GIBSON and O. F. NOLAN. Suprapubic prostatectomy.

J. R. DILLON. Treatment of chronic pyelitis and pyelonephritis; treatment of cancer of prostate; technical improvements in surgical treatment of undescended testicle.

W. E. STEVENS. Unusual pathological conditions of the urinary tract in women.

EDGAR POTH. A new aseptic technique for uretero-enterostomy; mechanism of ascending infection of the urinary tract; experimental observations.

SIDNEY OLSEN. Tuberculosis of the genito-urinary tract; urinary calculi.

CLARK M. JOHNSON. Trauma of the genito-urinary tract; infections of the genito-urinary tract; renal and pararenal infections; renal anomalies.

L. P. PLAYER. Kidney lavage.

W. A. CARROLL. Ureteral lithiasis; rupture of kidney.

T. O. POWELL. Newer knowledge of tumors of the testicle with special reference to gonadotropic hormone excreted in the urine.

M. R. OTTINGER, LLOYD R. REYNOLDS and J. B. MCNAUGHT. Torek operation for undescended testicle; torsion of testicle.

GEORGE W. HARTMAN. Hematuria and pyuria; renal tuberculosis.

W. A. SUMNER. Relationship of chronic infections to lesions of the genito-urinary tract.

LEWIS MICHELSON. Obstruction of the neck of the bladder in the female.

R. GLENN CRAIG. Ureteral pain of obscure origin.

MORRELL VECKI. Renal movability.

ENDOCRINOLOGY

R. F. ESCAMILLA. Consideration of abdominal pain of endocrine origin.

SAMUEL COHN and F. I. HARRIS. Discussion of the treatment of undescended testicle by operation and glandular extracts.

LEO STANLEY. Endocrinology in a penal institution.

ORTHOPEDIC SURGERY

GEORGE J. MCCHESNEY, W. COX and R. L. DRESEL. Fracture of neck of femur; treatment without external splinting.

L. D. PRINCE, A. B. SIRBU and D. D. CHARMACK. Fractures of os calcis; replacement of tibial shaft by fibula following osteomyelitis; treatment of bursitis.

R. L. WAUGH. Clinical demonstration of Roger Anderson "Ought-O-Matic" splint and skeletal traction and countertraction methods applicable to Thomas or Hodgen splints.

LEROY C. ABBOTT. The shoulder joint.

JOHN B. DE C. M. SAUNDERS. The shoulder joint.

J. F. RINEHART. Vitamin C deficiency in arthritis.

KEENE HALDEMAN and JOHN B. DE C. M. SAUNDERS. Demonstrations of bone growth.

FRANCES BAKER. Heat therapy.

F. A. LOWE. Internal derangements of knee joint, clinic and motion picture demonstration; fracture of humerus, clinic and motion picture demonstration.

J. J. LOUTZENHEISER. Arthrodesis of foot.

S. L. HAAS. Application of Hibbs-Risser plaster for scoliosis; results of treatment for scoliosis; results of tendon transplantation; Legg-Perthes disease.

J. J. SALE, W. O. MONTGOMERY, V. M. DILLON and W. J. COX. Industrial surgery and orthopedics.

J. H. O'CONNOR. Reduction of complicated fractures, closed methods, demonstration of cases, indications for open reduction.

C. A. WALKER. End-results of open reduction of fractures; treatment of compression fractures of spine, 250 cases; fractures of clavicle and patella.

W. W. WASHBURN. Disabilities following fractures, factors influencing period of recovery.

LEONARD W. ELY. Arthritis of the hip.

D. KING. Functional anatomy and pathology of the shoulder joint.

A. L. FISHER. Treatment of flat feet.

MERRILL C. MENSOR. Osteogenic sarcoma of spine; relation of bacteriophage to the Orr treatment of osteomyelitis.

NELSON J. HOWARD. Traumatic lesions of bursæ, tendons and muscles.

LEON PARKER. Familial tendencies in Paget's disease.

D. KING. Treatment of chronic sclerosing osteomyelitis.

F. G. LINDE. Compression fractures of spine; non-union of fractures.

F. C. BOST. Hibbs-Risser treatment of scoliosis; dislocation of carpal semilunar; fracture of ankle; ligamentous tears of ankle; treatment of fracture of os calcis.

W. J. COX. Internal derangement of knee joint, rupture of ligaments; treatment of fracture of femoral neck with Smith-Peterson nails.

KEENE O. HALDEMAN. Pathology of acute osteomyelitis; pathology of chronic infections of bone.

RALPH SOTO-HALL and KEENE O. HALDEMAN. Fracture dislocation of cervical spine; Duncan's traction apparatus.

PAUL E. JOHNSON, B. H. HENNING and JOHN A. KENNEDY. Disability ratings of Veterans Administration for orthopedic conditions of the extremities.

CARLETON MATHEWSON, JR. and J. B. MCNAUGHT. Treatment of spiral fractures of tibia; open and closed methods of treatment of fractures of extremities; tuberculosis of pelvis.

D. KING, J. M. MEHERIN and R. A. SCARBOROUGH. Fracture of the carpal scaphoid; surgical approaches to bones and joints; the Orr method of treatment of osteomyelitis.

NELSON J. HOWARD. Fractures of the upper end of the humerus, motion picture demonstration.

MERRILL C. MENSOR and LEON PARKER. Unusual fractures of the spine; treatment of osteomyelitis with surgical maggots.

C. C. MCRAE. Injuries of small bones of the hand.

EDGAR L. GILCREEST. Problems in treatment of fractures.

SURGERY OF THE GASTRO-INTESTINAL TRACT

HAROLD BRUNN. Cancer of rectum.

F. I. HARRIS. Cicatrizing (chronic) enteritis (regiona ileitis); treatment of appendix stump, noninversion.

FRED H. KRUSE. Common complications of peptic ulcer.

E. J. BEST, F. H. KRUSE, THEODORE ALTHAUSEN and RALPH RABINOWITZ. Postoperative care of intestinal conditions.

M. F. CUNHA. Primary duodenitis; end-results of ulcer cases, types of operation, causes of recurrence.

LEON GOLDMAN and THEODORE ALTHAUSEN. Pseudo perforation of peptic ulcer.

J. HOMER WOOLSEY and H. GLENN BELL. Carcinoma of stomach.

M. L. MONTGOMERY and JOSEPH M. SWINDT. Acute intestinal obstruction, experimental and clinical.

H. GLENN BELL. Subacute intestinal obstruction, localized type (chronic cicatrizing enteritis).

H. GLENN BELL and LEON GOLDMAN. Congenital lesions, tumors, diverticula of small bowel.

M. S. WOOLF, LEON GOLDMAN and H. GLENN BELL. Carcinoma of large bowel.

DUDLEY SMITH and J. W. MORGAN. Carcinoma of rectum.

ASA W. COLLINS. Pylorectomy and gastro-enterostomy.

LEROY BROOKS. Diagnosis and treatment of intestinal obstruction.

P. K. BROWN. Peptic ulcer, indications for surgical treatment.

W. W. WASHBURN. Acute perforation of peptic ulcer, complications and end-results in 100 cases.

ERNST GEHRELS. Radical surgery for gastric and duodenal ulcers; diverticulitis of colon; closure of colostomy; preservation of anal sphincter.

J. A. GUILFOIL. Chronic appendicitis, end-results of operation.

J. E. BOHM. Mortality rate of operations for appendicitis.

R. A. SCARBOROUGH. Developments in surgical treatment of carcinoma of rectum, 200 cases.

EMILE HOLMAN. Causes for failure to control symptoms and to prevent gastrojejunal ulcer in gastric surgery.

GUNTHER W. NAGEL, F. L. REICHERT and MARY E. MATHES. Chronic regional enteritis, clinical, experimental.

DAVID A. WOOD. Multiple primary carcinomata of colon complicating multiple polyposis of colon.

NELSON J. HOWARD. Amebic granuloma of large bowel.

HAROLD BRUNN. Carcinoma of large bowel; carcinoma of rectum; bowel obstruction.

GEORGE K. RHODES. Spontaneous perforation of cecum from obstruction in distal colon.

DANIEL SOOY. Choice of operation in gastric surgery.

EDWARD TOPHAM. End-results in surgery for gastric ulcer.

H. P. HILL, GEORGE BARNETT, J. M. MEHERIN, J. W. CLINE, JR., CARLETON MATHEWSON, JR., J. B. MCNAUGHT and A. C. MCKENNEY. Lesions of the upper gastro-intestinal tract; amebic infections of liver and gastro-intestinal tract.

DUDLEY SMITH. Operation for rectal fistula and hemorrhoidectomy, motion picture demonstration.

ASA W. COLLINS. Operations on the stomach, particularly pylorectomy and gastro-enterostomy.

THORACIC SURGERY

HAROLD BRUNN, A. L. BROWN, H. ROSENBLUM and J. J. SAMPSON. Symposium on surgery of the heart with particular reference to adhesive pericarditis.

LEO ELOESSER, PHILIP H. PIERSON, W. L. ROGERS, W. G. BURKHARD, DAVID A. WOOD, W. R. CLARK and L. H. GARLAND. Various types of bronchial stenosis; mycotic infections of the lung; tumors of the lung; empyema.

EMILE HOLMAN. Technical improvements in partial selective thoracoplasty; resection of transverse process; resection of scapula; ligation of the pulmonary artery as a therapeutic measure in pulmonary hemorrhage; carcinoma of lung simulating inflammatory disease.

HAROLD BRUNN, SIDNEY J. SHIPMAN, H. BRODIE STEPHENS, A. L. BROWN, M. W. DEBENHAM and A. GOLDMAN. Lung suppurations; empyema; artificial pneumothorax; phrenic avulsion; thoracoplasty.

ALANSON WEEKS and G. D. DELPRAT. Thoracoplasty.

RAY KISTLER. Diaphragmatic hernia.

SIDNEY J. SHIPMAN. Pneumothorax in pneumonia.

W. B. FAULKNER, JR. Bronchiectasis; treatment of chest injuries.

A. L. BROWN. Collapse therapy in pulmonary tuberculosis.

S. SHERMAN. Lymphoblastoma of mediastinum.

C. A. WALKER. Phrenicectomy for pleuropericardial adhesions.

A. GOLDMAN. Staphylococcic infections of the lung; chemotherapy in tuberculosis.

T. F. MULLEN. Antethoracic esophagoplasty.

MARY E. MATHES. Experimental study of the effect of various pathological conditions upon the dual blood supply of the lungs.

EDGAR POTH. A simple apparatus for tidal and siphon irrigation and its application in treatment of empyema.

DAVID A. WOOD and MARY E. MATHES. Exhibit of clinical and experimental observations on the dual blood supply of the lungs in various pathological states.

LLOYD B. CROW. Pulmonary infarct.

GYNECOLOGY AND OBSTETRICS

WILLIAM G. MOORE. Endometriosis; fibromyomata of uterus.

A. M. VOLLMER. Rubin's insufflation test; trichomonas vaginalis.

R. K. SMITH. Classical cesarean section, motion picture demonstration.

FRANK LYNCH, ALICE MAXWELL and R. S. STONE. Uterine cancer, follow-up, X-ray therapy, radium therapy.

MARGARET SCHULZE. Special ovarian tumors.

A. H. HEALD and ALICE MAXWELL. X-ray pelvimetry, direct method.

PHILIP H. ARNOT. Conduct of labor in posterior position.

LUDWIG EMGE. Dysmenorrhea, causes and treatment; sterility, diagnosis and treatment.

C. F. FLUHMANN, P. E. HOFFMAN and GERTRUDE F. JONES. Endocrinological aspects of gynecology, modern methods of diagnosis, blood and urine hormone tests, biopsy of endometrium, hormone therapy.

A. V. PETTIT. Results of hyperpyrexia in treatment of acute and chronic pelvic inflammatory disease.

LUDWIG EMGE. Radiation therapy of carcinoma of cervix, methods and end-results.

A. M. VOLLMER. Treatment of abortions.

MARGARET SCHULZE. Multiple pregnancies; pyelitis with pregnancy; hydatidiform mole and chorio-epithelioma; cardiac disease with pregnancy.

KARL L. SCHAUPP. Fibromyoma of the uterus.

HANS VON GELDERN. Plastic operations on pelvis.

C. L. COOLEY. Demonstration of gynecological cases.

R. D. DUNN. Treatment of incomplete abortions.

D. A. DALLAS. Operations in obstetrics.

BEVERLY SIMPSON. Separated placenta.

ADOLPH E. SCHMIDT. Uterine bleeding.

SURGERY OF THE BILIARY TRACT, LIVER AND PANCREAS

ALANSON WEEKS and G. D. DELPRAT. Common duct stone; hydatid disease of liver; granuloma inguinale.

F. I. HARRIS. Acute cholecystitis.

CARL HOAG. Reconstruction of common duct.

H. CLARE SHEPARDSON and HANS LISSER. Pancreatic dysfunction; hypoglycemia.

H. GLENN BELL and THEODORE ALTHAUSEN. Operative mortality and pre-operative management of cholecystitis, glucose therapy, Rose-Bengal and other tests.

FRED H. KRUSE and THEORDORE ALTHAUSEN. Medical and surgical jaundice; cirrhosis of liver, differential diagnosis from carcinoma of stomach.

JESSE L. CARR and FREDERICK S. FOOTE. Experimental work in human jaundice.

KARL SCHMIDT. The bile salts.

EMILE HOLMAN. Postoperative and inflammatory stenosis of the bile passages.

M. W. DEBENHAM and J. M. SWINDT. Liver abscess.

STANLEY H. MENTZER. Acute cholecystitis; obstructive cholecystitis.

RODNEY A. YOELL. Gall-bladder anomalies.

T. F. MULLEN. Recurrence of symptoms after surgery.

CIRCULATORY DISEASE

M. L. MONTGOMERY. Therapeutic venous occlusion.

C. A. NOBLE, JR. Postoperative cardiac versus circulatory collapse.

NEUROSURGERY

HOWARD C. NAFFZIGER. Late results in the treatment of malignant exophthalmos; brain tumors; factors influencing recovery after peripheral nerve injury; cervical ribs, "scalenus syndrome without cervical ribs."

HOWARD W. FLEMING. Subdural hematomata; cerebrospinal rhinorrhea; relief of intractable pain; cranial approach for orbital tumors; craniocerebral injuries.

EDMUND MORRISSEY. Neurologic clinic on lesions of the cauda equina; diagnosis and treatment of subdural hemorrhage; diagnosis of subdural hemorrhage.

O. W. JONES, JR. Spinal cord tumors.

H. A. BROWN. Low back injuries; spinal cord injuries.

E. B. TOWNE. Treatment of acute head injuries.

F. L. REICHERT. Neuralgias of cranial nerves, demonstration of patient and lantern slides.

ROBERT AIRD. Encephalography, clinical, experimental; intradural alcohol injections for intractable pain.

E. B. TOWNE, E. MORRISSEY, J. W. WOLFSOHN and D. WOOD. Surgical lesions of the spinal cord; dynamics of epilepsy.

L. B. LAWRENCE. Spinal cord tumors; tumors of cauda equina.

LEE HAND. Regeneration of peripheral nerves of hand.

EDMUND J. MORRISSEY. Diagnosis and treatment of subdural hemorrhages.

SURGERY OF INFECTIONS

A. S. WHITE. Treatment of staphylococcus infections with staphloid.

S. A. GOLDMAN. Studies on staphylococcus infections.

F. J. MCCARTHY. End-results in infections of the hand.

B. F. ALDEN. Relation of focal infection to Wassermann-fast lues.

V. H. MITCHELL. Treatment of anaerobic infection of the extremities, presentation of cured patients.

CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

ALAMEDA COUNTY HOSPITAL

WHITFIELD CRANE and W. EARL MITCHELL—9. Carcinoma of stomach.

FRANK H. BOWLES and THEODORE LAWSON—10. Carcinoma of rectum.

H. W. HARDING and DON D. WEAVER—11. Carcinoma of colon.

LEMUEL P. ADAMS—12. Carcinoma of breast.

SUMNER EVERINGHAM—9. Extrapleural thoracoplasty; intrapleural pneumolysis; clinic on phrenic interruption and thoracoplasty. Discussion by CHESLEY BUSH.

WARREN B. ALLEN—12. Neurosurgery.

W. F. HOLCOMB—9. Arthroplasty of hip.

L. B. BARNARD—10. Arthroplasty of shoulder.

E. N. EWER—9. Total hysterectomy; subtotal hysterectomy; discussion of obstetrical service at Alameda County Hospital.

CLARENCE A. DEPUY—11. Gynecological cancer clinic. Demonstration of intraspinal alcohol injection and presentation of cases.

ALBERT M. MEADS, LLOYD KINDALL, JOHN A. DAUGHERTY, T. I. BUCKLEY and associates—9. Perineal prostatectomy, suprapubic prostatectomy, resectoscopic prostatectomy. Operations, demonstration of cases and discussion.

Dry Clinics, 2—4:30

CHARLES A. DUKES and associates. Cancer clinic.

HAROLD H. HITCHCOCK, N. A. CARY and associates. Traumatic and orthopedic clinic; demonstration of Sweetland cast dryer, Bell table, plaster models, splints, etc.

W. H. SARGENT and C. B. BOWEN. X-ray exhibit and discussion.

GERTRUDE MOORE. Pathological exhibit and conference.

BERKELEY GENERAL HOSPITAL

Dry Clinics, 9—12

FRANK D. WALSH. Cholecystitis, observations and comments on surgical treatment.

CLAUDE H. CHURCH. Ectopic pregnancy recurring on same side.

WILLIAM W. CROSS. Polycystic kidney; nephrolithiasis; prostatic management.

J. F. CARLSON. Osteochondromatosis involving all epiphyses in one extremity; clavicle dressings.

W. W. REICH. Parathyroid disease, gross specimens and microprojections.

R. G. VAN NUYS. X-ray demonstration and discussion.

CHILDREN'S HOSPITAL

ROY NELSON—9. Demonstration of methods of treatment of esophageal stricture due to lye.

W. W. CROSS—9. Postmortem findings in the kidneys of children, lantern slide demonstration.

CLIFFORD SWEET—9. Clinic on undescended testes: Demonstration of postoperative results; discussion of the effect of antuitrin S; demonstration of operation.

ALTA BATES HOSPITAL

Staff—9. Operations and dry clinics.

SAMUEL MERRITT HOSPITAL

WARREN B. ALLEN—9. Reconstruction of skull defects, operation and demonstration of cases.

W. F. HOLCOMB and D. D. TOFFLEMEIER—9. Orthopedic operations and demonstrations.

MARK L. EMERSON—9. Rectal surgery and presentation of cases.

FRANK H. BOWLES—9. Thyroidectomy.

W. H. SARGENT—9. X-ray demonstration and discussion of cases.

ROBERT A. GLENN—9. Pathological exhibit; demonstration of frozen section technique and specimens.

WHITFIELD CRANE—10:30. Peptic ulcer; Judd pyloroplasty.

W. EARL MITCHELL—10:30. Pelvic tumor.

HENNING KOFORD—10:30. Cholecystectomy.

CHARLES A. DUKES—11. Apicolysis, operation; demonstration of thoracic cases. Discussion by HAROLD TRIMBLE.

H. N. ROWELL, A. M. SMITH, W. H. STRIETMANN, A. A. ALEXANDER, W. S. KUDER, STEWART V. IRWIN, H. GORDON MACLEAN, FLETCHER B. TAYLOR, VERNE G. ALDERSON and HOBART ROBERTS—2. Symposium on pre- and postoperative care: Management of surgical jaundice and stomach cases; diabetes in surgery; traumatic and postoperative pneumonia; cardiac and renal complications; postoperative psychosis; allergy in relation to abdominal surgery; discussion and demonstration of cases.

PERALTA HOSPITAL

J. L. LOHSE—9. Cholecystectomy.

ERGO A. MAJORS—9. Carcinoma of breast, radical removal.

F. M. LOOMIS and JOHN W. SHERRICK—9. Porro cesarean section.

CHARLES B. FOWLER—9. Orthopedic treatment of spondylolisthesis; correction of upper extremity involvement in poliomyelitis.

H. J. TEMPLETON and J. LUNSFORD—10. Electric desiccation in cutaneous malignancies.

JOHN W. SHERRICK—10. Vaginal plastic.

T. FLOYD BELL—10. Pelvic tumor.

T. C. LAWSON—11. Hernia, fascial repair.

P. N. JACOBSEN—11. Bladder surgery.

PAUL MICHAEL—9 to 1. Pathological demonstration and exhibit.

J. D. COATES—9 to 1. X-ray demonstration and exhibit.

COWELL MEMORIAL HOSPITAL

HERBERT EVANS, ROBERT LEGGE, C. A. KOFOID and associates—9. Exhibit and discussion of latest advances in endocrinology; inspection of laboratories and hospital with special reference to the systematic medical care of university students; discussion of laboratory technique with particular reference to amebiasis.

ALAMEDA SANATORIUM

J. OHANNESON—9. Hernioplasty under local anesthesia; appendectomy.

G. R. BURKE—9. Cholecystectomy.

CHANNING HALL—10. Resection of stomach.

PROVIDENCE HOSPITAL

O. D. HAMLIN—9. Intestinal anastomosis.
J. RADFORD FEARN—9. Vaginal hysterectomy under local anesthesia.
A. REIS—10. Cholecystectomy, new method.
THEODORE M. WELLER—10. Cesarean section.
N. AUSTIN CARY—11. Sacro-iliac fusion.
PHILIP J. DICK—11. Posterior gastro-enterostomy.
MICHAEL TORRANO—12. Herniotomy under local anesthesia.
S. A. JELTE—9 to 12. X-ray demonstration and discussion.

EAST OAKLAND HOSPITAL

DON D. WEAVER—9. Ulcer of the stomach.
O. R. ETTER—9. Surgery in the diabetic patient, dry clinic.
R. G. VAN NUYS—10. Dry clinic: Visceroptosis and position of the viscera in healthy young adults; X-ray demonstration.
BROOKS STEPHENS—10:30. Hallux valgus.
CLAIR RASOR—10:30. Prolapse of uterus.
ALEXANDER H. GRIFFITH—11. Carcinoma of the recto-sigmoidal juncture, Lahey technique.

SURGERY OF THE EYE, EAR, NOSE, AND THROAT

CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

UNIVERSITY OF CALIFORNIA HOSPITAL

Tuesday

JOSEPH L. MCCOOL, FREDERICK C. CORDES, JOSEPH W. CRAWFORD, C. ALLEN DICKEY and DAVID O. HARRINGTON—9. Ophthalmological operations.
R. C. MARTIN and FREDERICK C. CORDES—9. Toti-Mosher operation.
WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9. Otolaryngological operations.

Dry Clinics—2

FREDERICK C. CORDES. Surgery of traumatic cataracts.
J. W. CRAWFORD. Tuberculosis of the eye.
C. ALLEN DICKEY. Surgery of the vertical muscles.
DAVID HARRINGTON. Contact glasses, practical demonstration.
R. C. MARTIN and STERLING BUNNELL. Injuries and repair of the facial nerve.

Thursday

JOSEPH L. MCCOOL, FREDERICK C. CORDES, JOSEPH W. CRAWFORD, C. ALLEN DICKEY and DAVID O. HARRINGTON—9. Opthalmological operations.
R. C. MARTIN and FREDERICK C. CORDES—9. Toti-Mosher operation.
WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9. Otolaryngological operations.

Dry Clinics—2

JOHN SAUNDERS. Regional anatomy of the mastoid and pathways of infection of the intracranium.
HOWARD C. NAFFZIGER. Brain abscess arising from middle ear and mastoid infections.
WALLACE SMITH. Phlebitis and thrombosis following middle ear and mastoid infections.

Friday—2

FREDERICK C. CORDES. Surgery of complicated cataracts.
J. W. CRAWFORD. The eye in diabetes.
C. ALLEN DICKEY. The value of orthoptic treatment.
DAVID HARRINGTON. Tobacco amblyopia and its treatment.

ST. MARY'S HOSPITAL

Thursday—2

FRANCIS CONLAN, STANLEY BURNS and FRANK HAND. Treatment of posterior sinusitis. Blood dyscrasias in relation to the ear, nose and throat. Treatment of bilateral abductor paralysis.
FRANK HAND. Radical antrum.

HOSPITAL FOR CHILDREN

Thursday—2

GEORGE N. HOSFORD and AVERY M. HICKS. Technique for the determination of the hydrogen ion concentration of tears. The significance of pH of tears in ocular symptoms and treatment. Indications for and results of orthoptic training. Relation of vertical imbalance of extra-ocular muscles to gastric symptoms, posture, temperament and aptitude for school work and occupation. Congenital muscle palsy. Motion picture demonstration of O'Connor technique for heterophoria and heterotropia.

Days to Be Announced

GEORGE N. HOSFORD and AVERY M. HICKS—9. Extraction of congenital cataract; muscle operations, O'Connor cinch shortening for simple exotropia, simple esotropia, vertical deviations; muscle transplants for external rectus palsy, superior rectus for paralysis of the superior oblique (Jackson's technique), Motais' operation for congenital ptosis; Toti-Mosher operation for occlusion of nasolacrymal duct (with Drs. Martin and Hosmer).

SAN FRANCISCO HOSPITAL

Tuesday—2

WARREN D. HORNER. External iridectomy; history, uses, technique and advantages.
C. ALLEN DICKEY and J. W. CRAWFORD. Safety procedures in cataract operations; akinesis, intra-orbital injections, lid sutures, pre-operative medication.
WARREN D. HORNER, C. ALLEN DICKEY and J. W. CRAWFORD. The use of synthetic epinephrin bitartrate in ocular therapeutics.
AUBREY RAWLINS. Osteoma of the antrum; some curious foreign bodies in the lungs; cases of recovery from otitic meningitis; extensive osteomyelitis of the frontal bone.
HARRINGTON B. GRAHAM. Foreign bodies in the lungs; stenosis of the esophagus; cancer of the larynx.
HARRINGTON B. GRAHAM and J. M. WOLFSOHN. Extensive abscess of the meninges.
RAE ASHLEY. Treatment of tuberculosis of the larynx.

STANFORD UNIVERSITY SCHOOL OF MEDICINE

Wednesday—2

FRANK RODIN. Congenital and hereditary eye defects.
AVERY HICKS. Ocular torticollis.
D. PISCHEL. Retinal detachment, methods and results.

MOUNT ZION HOSPITAL

Tuesday

HERBERT J. COHN, EDWARD LIPSETT and JOHN SKAFF—9. Tonsil operations, local and general anesthesia, dissection, Sluder, snaretome.

Wednesday—2

HERBERT J. COHN, EDWARD LIPSETT and JOHN SKAFF. Symposium on mastoidectomy.
GEORGE S. LACHMAN. Treatment of corneal ulcers.
CHARLES WEISS. Recently developed concepts in immunology and bacteriology of value to the ophthalmologist.
FRANK H. RODIN. Treatment of acute ridocyclitis.
G. Y. RUSK. Pathological demonstration of various eye conditions.

Thursday

Staff—9. Nasal operations: Submucous resection, electrocoagulation of turbinates, sinus surgery.

Days to Be Announced

FRANK H. RODIN and GEORGE S. LACHMAN—9. Ophthalmological operations: Cataract, strabismus, plastic on eyelids.

SOUTHERN PACIFIC HOSPITAL

Thursday—2

WILBUR F. SWEET and JOHN C. WILLIAMS. Clinics and demonstration of cases.

LETTERMAN GENERAL HOSPITAL

Tuesday

A. E. SCHLANSER and HERBERT H. PRICE—9. Tonsillectomies; adenoidectomies, general anesthesia.
HARVEY C. MAXWELL—9:30. Eye surgery, general anesthesia: Strabismus correction by O'Connor tendon cinch and by Jamieson recession.

Wednesday

A. E. SCHLANSER—9. Tonsillectomies, local anesthesia; nasal operations, local anesthesia.

Thursday

HARVEY C. MAXWELL—9. Eye operations, local anesthesia; cataract extraction, pterygium transplant, strabismus correction.

Friday

A. E. SCHLANSER, HERBERT H. PRICE and HARVEY C. MAXWELL—9. Sinus surgery, local anesthesia; extranasal radical frontal ethmosphenoidectomy; radical maxillary sinusotomy; bronchoscopy; esophagoscopy.

ST. LUKE'S HOSPITAL

Tuesday and Thursday

JOSEPH L. MCCOOL, C. ALLEN DICKEY, A. E. EDGERTON and CHARLES BATES—9. Ophthalmological clinic.

VETERANS ADMINISTRATION

Staff. Bronchoscopic examinations.

CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

PROVIDENCE HOSPITAL

A. J. HOWELL—9. Reconstruction of nose.
RODERIC O'CONNOR—9. Muscle shortening; cataract; Curran operation.
GEORGE MCCLURE and NELSON KEELER—9. Ear, nose and throat surgery.
RANDOLPH SHARPSTEEN—9. Motais' operation.
ROY NELSON—9. Esophagoscopy and bronchoscopy.
BRUCE STEPHENS, JR.—10. Cataract operation.
FRANK BAXTER—10. Ear, nose and throat operations.
MILTON H. SHUTES—10. Ear, nose and throat operations.
ALEXANDER GALBRAITH—10. Ear, nose and throat operations.
W. A. MAGRATH—11. Eye operations.
ALVIN P. WOLD—11. Eye surgery.
F. C. KRACAW—11. Ear, nose and throat surgery.
R. J. NUTTING—12. Eye operations.
P. T. LEFTWICH—12. Ear, nose and throat surgery.
FRANCIS SHOOK—12. Ear, nose and throat surgery.
SYDNEY N. PARKINSON—12. Treatment of acute and subacute paranasal sinus infections, lantern slides and motion picture demonstration.

Dry Clinic, 2—4-30 p. m.

Staff. Discussion of operative procedures, demonstration of cases, lantern and motion picture demonstration.

ALAMEDA SANATORIUM

B. M. STEPHENS—11. Cataract.

CHILDREN'S HOSPITAL

M. E. LANDO—10. Strabismus, operative treatment.

UNIV. OF ILL.

Fig. 1. Early hypertrophic stage.

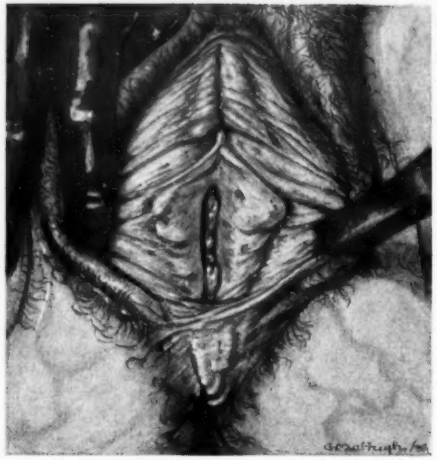


Fig. 2. Second stage, moderate atrophic changes.

Fig. 3. Third stage, advanced atrophy.

Chronic Atrophic Dermatitis of the Vulva.—Fred L. Adair and Edward M. Davis.